DEVELOPMENTAL OUTCOME FOR PRESCHOOLERS PRENATALLY EXPOSED TO CRACK COCAINE: BEHAVIORAL AND ADAPTIVE SEQUELAE

By

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TABLE OF CONTENTS

LIST OF TABLES

Abstract of the Dissertation Presented to the Graduate School of the University of Florida in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy

DEVELOPMENTAL OUTCOME FOR TODDLERS PRENATALLY EXPOSED TO CRACK COCAINE: BEHAVIORAL AND ADAPTIVE SEQUELAE

By

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Early studies indicated that infants exposed prenatally to cocaine and cocaine derivatives may be at risk for increased spontaneous abortions, fetal death, preterm labor, abruptio placentae, decreased length, weight, and head circumference, congenital malformations, and deviant neurobehavior. However, very little long-term followup has been done to assess the functioning of these children as they mature. The present study compared two groups of three-year old preschoolers who were a) exposed in utero to crack, or b) not exposed in utero to crack. Information about child behavior and adaptive functioning was collected by primary caregiver report using the Vineland Adaptive Behavior Scales Survey Form, the Connors Parent Rating Scale, and the Eyberg

Child Behavior Inventory. Child behavior was also assessed by direct objective observation using the Dyadic Parent-Child Interaction Coding System-II. Administered instruments intended to determine whether a) scores for the total sample conformed to norms provided by psychological measures, and b) whether behavioral or adaptive deficits were present in the crack-exposed preschoolers when compared to same-aged nonexposed peers. Results showed significant differences between the total study cohort which included exposed and nonexposed children and normative groups on which many standardized psychological measures are based. For example, the total sample was more likely to display elevations in conduct problems, learning problems, hyperactivity, and impulsivity compared to normative groups. Second, at three years of age, no differences were found between a prenatally crack-exposed cohort on parent and objective measures of behavior and adaptive functioning when compared with nonexposed matched peers. Thus elevations on disordered behavior compared to normative groups cannot be attributed to exposure status. Implications of findings and possible explanation for nonsignificant between groups findings are discussed.

INTRODUCTION

Cocaine is one of the most popular illicit drugs used in the United States. Approximately 30 million Americans have tried cocaine at least once and as many as five million use cocaine on a regular basis (Abelson & Miller, 1985). The two common forms of illicit cocaine are cocaine hydrocholoride (HCl) in a powder form, and 'crack,' a highly purified alkaloidal base also known as 'freebase.'

Cocaine (methylbenzoylecgonine) is a central nervous system (CNS) stimulant that works in part by increasing the activation of the neurotransmitter dopamine in the mesolimbic and/or mesocortical pathways. Increased activation results in a stimulant induced reward or the 'euphoria' commonly experienced by cocaine users (Goeders & Smith, 1983; Wise, 1984). Neurotransmitter reuptake is simultaneously reduced in the cerebral cortex, hypothalamus, and cerebellum resulting in the hyperaroused state also typical of cocaine intoxication (Ryan, Ehrlich, & Finnegan, 1987). Cocaine taken intranasally (or 'snorted') causes vasoconstriction of the nasal mucous membranes which reduces its own absorption. Subsequently, the plasma drug concentration rises relatively slowly for

insufflatted cocaine. Cocaine in powder form is also frequently diluted or cut before sale further limiting plasma drug concentrations in the body.

Crack on the other hand is almost 70% pure cocaine, made by precipitating alkaloidal cocaine from an aqueous solution of cocaine HCl. Unlike the powder form of cocaine, crack is not destroyed by moderate heating and vaporizes at temperatures over 98 degrees celcius (Medical Letter, 1986). Crack, named for the popping sound it makes when heating, may be smoked via freebasing with a base pipe or rolled with tobacco in a cigarette. Crack may also be injected. Smoking crack delivers large quantities of cocaine directly to the vascular bed of the lungs. The plasma drug concentration in this instance is substantially higher than for insufflatted cocaine and rises almost instantaneously producing an effect more intense than that experienced with intravenous injection (Medical Letter, 1986).

Crack when smoked reaches the brain in approximately eight seconds producing an intense, immediate euphoria (Howard, Mofenson, & Caraccio, 1987). These euphoric effects are short lived, lasting approximately 45 minutes followed by a severe crash (dysphoria) during which the user becomes depressed and agitated (Howard, 1989). This cycle is

reportedly shorter and more intense when smoking crack than for either intranasally or intravenously administered cocaine. Users may feel a greater compulsion to repeat the experience when smoking crack both for its magnified euphoric effects as well to avoid the subsequent crash (Howard et al., 1987). Binges, characterized by frequent readministration of the drug, reportedly may last 12 hours but may go on for several days (Gawin & Kleber, 1985). In addition, the price of crack continues to decrease, making it accessible to people of all socioeconomic levels. A 'rock' may cost as little as five to ten dollars (Howard, 1989). Combined, these factors precipitate abuse.

While it is uncertain whether cocaine is physically addictive, it clearly has powerful psychological effects. It is estimated that five times as many people are addicted to cocaine than to heroin (Grinspoon & Balkalar, 1980). Indeed, treatment for cocaine use, and crack use in particular, is escalating while age of first use appears to be dropping (Adams, Gfroerer, Rouse, & Kosel, 1986). In reaction to epidemic use, researchers are beginning to describe not only the immediate effects of cocaine intoxication but also to contemplate the long-term implications of using what had

initially been considered a 'safe' stimulant (Schnoll, Karrigan, Kitchen, Daghestani, & Hansen, 1985; Siegel, 1985).

Associated with the use of cocaine are a number of behavioral changes as well as substantial physical risk. Behavioral effects that have been described in adult users include impulsivity, disinhibition, repetitive actions, anxiety, psychomotor activation and a loss of appetite which can result in malnutrition (Howard et al., 1987; Levine, Washington, Jefferson, Kieran, Moen, Feit, & Welch, 1987; Medical Letter, 1986). Severe and toxic physiological effects have been described in the literature. Hypertension, tachycardia, ventricular arrhythmias, seizures, loss of consciousness, stroke, and myocardial infarctions are increasingly attributed to cocaine use. Even deaths due to respiratory and cardiac arrest have been reported (Howard et al., 1987; Levine et al., 1987; Medical Letter, 1986).

Further, there are indications that the inhibitory receptors of dopamine neurons become supersensitive as an adaptation to chronic activation of the reward pathways which occurs with stimulant use (Gawin & Kelber, 1986). Thus, there is some evidence that long-term cocaine use may lead to permanent neurophysiological changes in the brain that impact on mood states and the user's experience of pleasure. Such

findings are mirrored in clinical observations of protracted anhedonia and anergia in some cocaine users (Gawin & Kleber, 1986). Generally, these symptoms resolve over time. However, there are sporadic reports of high dose users with chronic anhedonia, anergia and a craving for stimulants that does not remit (Ellinwood, 1974; Schuster & Fischman, 1985).

Pregnant women are not immune to either the pleasurable effects of crack or to the physiological consequences of use. Over the last several years researchers have turned their attention to the possible impact of in utero exposure to cocaine and cocaine derivatives on the neonate. This interest has accelerated due partially to shifting attitudes towards drug use in general as well as justified alarm at the recent explosion in crack use (Grinspoon & Balkalar, 1980). Still, the toxic effects of cocaine use are only beginning to be understood, and focus has been almost entirely on adult users. Early reports concerning infant outcomes of in utero exposure to cocaine has been limited, often anecdotal, contradictory and predominantly focused on medical outcomes (Ryan et al., 1987) Thus, while reports in the popular media of antisocial or hyperactive toddlers created by in utero exposure to cocaine make sensational copy, they are distinctly premature.

Research, medical or otherwise, on preschoolers exposed to cocaine in utero is very limited.

The absence of literature notwithstanding, concern for a generation of children exposed to cocaine is certainly warranted. One survey suggested that 10% of women may use cocaine at least once during pregnancy, and 50% of these use other drugs in addition to cocaine (Howard et al., 1987). Cocaine is highly water and lipid soluble and passes through the placentae by simple diffusion. Cocaine may concentrate in the fetus because fetal blood has a lower pH. In addition, plasma cholinesterase, which is necessary to metabolize cocaine, is less active in the fetus and in pregnant women (Bingol, Fuchs, Diaz, Stone, & Gromisch, 1987). Conceivably, even small doses of cocaine could have negative consequences on a developmentally vulnerable embryo and fetus. Although results in the literature are equivocal, cocaine has been implicated in a number of negative outcomes including spontaneous abortions, fetal death, preterm labor, precipitous labor, abruptio placentae, fetal distress, fetal meconium staining and other conditions which qualify the newborn for high risk status (Chasnoff, Burns, Schnoll, & Burns, 1985; Oro & Dixon, 1987; Ryan et al., 1987).

Exposed infants have also been shown to exhibit decreased length, weight and head circumference, higher rates of congenital malformations, deviant neurobehavior, rapid shifts between irritability and lethargy, and be at increased risk for Sudden Infant Death Syndrome (SIDS) although many of these outcomes remain controversial (Bingol et al., 1987; Chasnoff, 1989; Chasnoff, Burns, & Burns, 1987; Oro & Dixon, 1987). However, negative findings are not consistently found in well controlled studies. Reports of investigations into the behavioral and long-term developmental outcome of cocaine-exposed infants remain unclear.

LITERATURE REVIEW

Physiological and Behavioral Effects

The physiological impact of in utero cocaine exposure has been extensively modelled in animal investigations. The underlying assumption in such studies is that cocaine may affect development in two principle ways: 1) by disturbing dopaminergic functioning in the developing fetus, and/or 2) via hypoxic effects.

The dopamine system is implicated in the modulation of reward systems, reinforcement, sensorimotor integration, and environmental responding. Cocaine acts as an inhibitor of dopamine reuptake presynaptically, serving to increase the amount of amines in the synaptic cleft. There is evidence that repeated cocaine administration decreases the amount of dopamine synthesis presynaptically and increases the number of dopamine receptors postsynaptically (Fung, Reed, & Lau, 1989). The dopaminergic system is developing in the third trimester of human fetal development and is functional and capable of mediating behaviors in rat fetuses towards the end of their gestational period. Moody, Robison, Spear, and Smotherman,

(1993) found that administration of cocaine to rat dams resulted in increases in fetal activity which they subsequently considered a reflection of altered CNS development.

Subsequent investigations found that prenatal exposure to cocaine in late gestation results in a decrease in the number of spontaneously active midbrain dopaminergic cells in adult rats, whereas rats exposed to cocaine only in adulthood showed an increase in the number of spontaneously active dopaminergic cells (Minabe, Ashby, Heyser, Spear, & Wang, 1992). The decrease of midbrain dopamine activity in adult rats exposed prenatally to cocaine has been used to explain early findings of irritability and decreased interactive behaviors in human infants. These reports suggest, not surprisingly, that prenatal cocaine exposure may be toxic to the fetus or impact negatively on the developing neuronal system in a manner that does not necessarily parallel consequences of adult exposure.

Studying cell development in brain regions, Seidler and Slotkin (1993) compared rat pups exposed in utero to cocaine during late gestation to a nonexposed comparison group. They found retarded maternal weight gain but no effect on pup body or brain region weights. DNA content was also largely unaffected. Although postnatal cell growth was reduced in the

forebrain, the magnitude of the reduction was small when compared to the impact of other drugs such as the hypoxic or ischemic effects of nicotine. Seidler and Slotkin (1992) concluded that functional deficits attributable to fetal cocaine exposure probably result from actions directed toward specific cell or synaptic populations as opposed to global effects on cell development.

In another investigation, Seidler and Slotkin (1992) found somewhat conflicting results when studying the effect of fetal cocaine exposure on rats given 30 mg/kg daily from gestational days 2 to 20. As a toxic referent, a dose of approximately 80 to 100 mg/kg of cocaine is generally fatal in adult rats. The exposed group showed minor differences from controls in body and brain region weights and in levels of norepinephrine. However, investigators found marked noradrenergic hyperactivity as assessed by noradrenergic turnover, which they attributed to the effects of glucocorticoids and hypoxia on noradrenergic cell differentiation. These results suggest that hypoxia rather than dopaminergic disruption may be the more critical result of cocaine exposure in utero.

Animals prenatally exposed to cocaine generally show differential physiologic responses to hypoxia compared to

controls. Weese-Mayer and Barkov (1993) studied the responses of rabbit pups to hypoxia following exposure to 30 mg/kg of cocaine from days seven to 15 gestation. They found the cocaine-exposed pups had more significant oxyhemoglobin desaturation and pulse deceleration during exposure to severe hypoxia than controls, suggesting that cocaine exposure in utero may reduce the normal defense mechanisms for metabolic adjustment to low oxygen.

These results supported findings from an earlier study by Weese-Mayer, Klemka-Walden, Barkov, and Gingras (1992) who also found that, while baseline ventilation did not differ significantly among study groups, cocaine-exposed pups had a deficient ventilatory response during an hypoxic challenge. Weese-Mayer et al. (1992) argued that these findings may represent perturbed maturation of respiratory control. Other researchers have found similar results which suggest that infants exposed to cocaine have an impaired repertoire of protective responses to hypoxia and hypercapnia during sleep which may play a role in increased risk for SIDS (Ward, Bautista, Woo, Chang, Schuetx, Wachsman, Sehgal, & Bean, 1992).

Similarly, Woods, Plessinger, and Clark (1987) found that pregnant ewes exposed to cocaine produced increases in

maternal blood pressure and decreases in uterine blood flow accompanied by fetal hypoxemia, hypertension, and tachycardia. Cocaine administration to the fetus directly resulted in relatively smaller increases in fetal heart rate and blood pressure than those observed following maternal administration, and no changes in fetal arterial blood gas values. These results were interpreted to indicate that maternal administration of cocaine alters fetal oxygenation by reducing uterine blood flow and impairing oxygen transfer to the fetus and that resulting fetal cardiovascular changes may reflect fetal hypoxemia, increased fetal levels of cocaine, or a combination of these events.

Birth outcome studies with animals demonstrate a range of postnatal results following cocaine exposure in utero. Henderson and McMillen (1990) studied postnatal development in rats exposed to cocaine daily in utero. The cocaine-exposed group weighed less, had more stillbirths, and more birth defects when compared to a nonexposed group. In addition, cocaine-exposed pups had delayed righting reflexes although no delay was noted in opening their eyes, both indices of developmental integrity. Their findings led Henderson and McMillen (1990) to conclude that cocaine exposure in utero

impacted neonatal outcome and long term development in the rats due to disruption of the dopamine system.

In a study designed to mimic moderate cocaine use by humans during pregnancy, Fung et al. (1989) examined the neurobehavioral responses and striatal dopaminergic system in cocaine-exposed newborn rats. No change in length of gestation, litter size, birth weight and length of pups, and the ratio of male to female pups was noted. At 14 days old, exposed and nonexposed pups showed similar locomotor performance in righting reflex, position reflex and negative geotaxic tests. Results demonstrated that prenatal exposure to cocaine did not alter the development of motor coordination suggesting no significant impact on the developing dopaminergic and striatal systems with moderate exposure.

Spear, Kirstein, Bell, Yoottanasumpun, Greenbaum, O'Shea, Hoffmann, and Spear (1989) also studied the early development of cocaine-exposed rats. They found that when pups were exposed a relatively large dose of cocaine daily (40 mg/kg) late in gestation, there were no differences in maternal weight gain, duration of pregnancy, or number of live male/female pups per litter were found. Like Fung et al. (1989), they found no differences in offspring body weights at birth and weaning, physical maturation and reflex development.

However, cocaine-exposed pups were deficient in learning and odor/milk association and showed enhanced locomotion. The researchers concluded that prenatal cocaine exposure impacts behavioral and cognitive function during the early postnatal period even in the absence of overt physiological changes.

A review of studies of postnatal integrity of animals exposed to moderate amounts of maternal cocaine administration reveals some consistencies. Generally studies have found no differences in dam weight gain, litter size or weight, or early postnatal behavioral tests (Smith, Mattran, Kurkjian, and Kurtz, 1989; Hutchings, Fico, & Dow-Edwards, 1989; Spear, Kirstein, & Frambes, 1989). However, drug effects have been noted on the level of locomotion, exploratory behavior, tail flick, footshock sensitivity and some learning and/or retention tasks. Arguments explaining significant results are generally dependent on altered neurodevelopment during critical prenatal periods, poor maternal nutrition, and hypoxia.

While animal models for cocaine exposure in utero may be useful, there are several difficulties in extrapolating the effects found in animals to humans. In addition to the obvious problem of equating human and rat, sheep, or rabbit neurodevelopment, results of animal studies also tend to vary

by species or strain. Furthermore, they appear to be heavily dose-dependent including some studies using extremely high doses of cocaine, and demonstrate that impact appears contingent upon the gestational period of drug administration. Clearly fetal exposure to cocaine is not a benign perinatal event. But the deficiencies noted in the animal literature such as locomotor changes or alterations in learning and "cognition" are frequently difficult to demonstrate in parallel forms in human infants. In addition, it is unclear whether such alterations in functioning found in the animal literature are transient or long-term.

Preliminary attempts have been made to study human infants in terms of the physiological impact of cocaine exposure in utero. For example, Link, Weese-Mayer, and Byrd (1991) performed magnetic resonance imagery (MRIs) on infants exposed to cocaine prenatally to determine the presence of hypoxic injuries. In all 21 infants studied, at a mean age of 3.6 years, they found myelination was appropriate compared to age-matched norms; brain and brainstem anatomy were also normal with no evidence of infarct or hemorrhage. Link et al. (1991) concluded that negative findings could be due to the small sample size, limited maternal use, or the possibility that cocaine use without concomitant use of other illicit

substances may not be as significant as some studies have suggested.

Doberczak, Shanzer, Senie, and Kandall (1988) likewise examined 39 infants with in utero exposure to cocaine for neurologic and electroencephalographic (EEG) abnormalities. During the first week of life, 17 of the infants had abnormal EEGs and abnormal behavior characterized by irritability. By the second week of life, nine of the 17 EEGs remained abnormal. By three to 12 months of age, however, findings had normalized, suggesting effects attributed to cocaine may be transient. There was no control group utilized in this study and it is unclear whether examiners were blinded to drug status. Despite these methodological flaws, it may be significant that EEG findings could not be predicted by neurologic dysfunction or perinatal variables, and ultimately, findings normalized for all infants.

Preliminary study of human infants indicates that cocaine exposure results in worse outcomes than nonexposed infants in terms of birth weight, length and head circumference, spontaneous abortion, fetal death, and sudden infant death syndrome (SID) (Ryan et al., 1987). In an early study, Oro and Dixon (1987) examined neonatal growth, behavior and physiologic organization in 104 mother/infant pairs including

a cocaine and methamphetamine group, a narcotic group and a drug free group. Findings in this study were plentiful and dramatic. The researchers found significantly lower birth weight, length, occipitofrontal head circumference (OFC), and gestational ages in both the cocaine/methamphetamine and narcotics groups compared to the illicit drug free group. They also found significantly higher incidence of prematurity, intrauterine growth retardation, fetal distress, and complications during the neonatal period in both the cocaine/methamphetamine and narcotics groups compared to the illicit drug free group.

Significant increases in neurologic and physiologic problems in the cocaine/methamphetamine group were also reported including (in order of decreasing significance) abnormal sleep patterns, tremors, poor feeding, hypertonia, vomiting, sneezing, high pitched crying, frantic fist sucking, tachypnea, loose stools, fever, yawning, hyperreflexia, and excoriation. Physician and nurse descriptions of the behavior of these exposed infants included disorganization, poor visual processing of faces and objects, random sucking and long dull-alert periods with eyes open. Decreased spontaneous activity and fixed catatonic postures were seen in four of the cocaine/methamphetamine group. Even accounting for various

maternal factors, cocaine/ methamphetamine and narcotic use still made significant independent and negative contributions to gestational age, birth weight, length and OFC (Oro & Dixon, 1987).

The results of this study and of many early studies like it appeared to confirm the clinicians' worse fears regarding cocaine exposure in utero. However, a critical evaluation of the methodology mitigates the findings to a degree. For example, in the above study, the combined effects of certain drugs (in this case methamphetamine and cocaine) may have had some unique or synergistic properties not found when the same drugs are taken separately. Further, it is unclear whether evaluators in this study were blinded to the drug group affiliation of the babies being studied. Confounds and researcher bias have been frequently apparent in this body of literature on prenatal cocaine exposure, especially in earlier reports.

In another study concerned with the teratogenic effects of cocaine, Bingol et al. (1987) compared a polydrug, a cocaine only, and a no illicit drug control group. The cocaine group was comprised of 60% intranasal, 30% free base inhalation, and 10% intravenous users. While no statistical differences were reported in the spontaneous abortion rates

among the three groups, stillbirth rates were significantly higher in the cocaine only group compared to the no drug group. Also, there were significantly more congenital malformations in the cocaine only group compared to both contrast groups. Five of fifty infants in the cocaine only group had major congenital malformations including exencephaly, intraparietal encephalocele, and parietal bone defects. Although complications occurred in women after all three routes of cocaine administration, the sequelae were more frequent in those who smoked crack regularly or injected it intravenously. These findings are dramatic and suggest that cocaine is a powerful teratogen to the developing fetus. However, this study was conducted in a large inner city hospital where the confound of polydrug use was common among the cocaine-using group, and it is unclear whether examiners were blinded as to the drug status of the infants.

Little, Snell, Klein, and Gilstrap (1989) also examined perinatal outcome following maternal cocaine use during pregnancy in 53 exposed infants compared to a 100 infant control group. Cocaine use in their study was associated with preterm labor; birth complications including meconium staining, tachycardia, and lower birth weight; and an excess of congenital cardiac anomalies. There were several

methodological shortcomings in this study which may impact the reliability of the authors' conclusions. Mothers were self reported drug users whose neonates were automatically referred to a high risk nursery for observation of withdrawal symptoms compromising blind evaluations. Furthermore, the cocaine-using mothers were generally older, more likely to be black, and use tobacco and other illicit drugs when compared to controls. Controls were not matched to drug using mothers, and it is unclear whether other risk variables were controlled adequately in the analysis.

In a subsequent study, Little and Snell (1991) studied the pattern of brain growth in cocaine-exposed newborn infants where brain growth was defined as head circumference in addition to other growth variables including birth weight, length, and gestational age. Groups were cocaine-exposed infants without alcohol exposure, alcohol but no cocaine exposure, and neither cocaine nor alcohol exposure. Results showed significant differences in head size between unexposed and cocaine-exposed infants. Head circumference was reduced proportionately more than birth weight in cocaine-exposed infants. Cocaine and alcohol exposed groups were not statistically different in terms of head size. Little and Snell (1991) concluded that cocaine exposure results in a

pattern of growth retardation similar to alcohol exposure and that this retardation may be asymmetrical with head size more involved. However, mothers in the cocaine group tended to be polydrug users, control groups were not matched, nor were statistical controls used for possible confounding maternal variables.

Chiriboga, Bateman, Brust, and Hauser (1992) reported that, compared to a no illicit drug exposure control group (n = 16), cocaine-exposed infants (n = 14) had significantly lower birth weights, lengths and head circumferences. Neurologic abnormalities were also associated with exposure and included hypertonia, plantar extension, tremors and gaze abnormalities. These findings led researchers to conclude that prenatal cocaine exposure results in tone and movement abnormalities in newborn infants. Strengths of this research were the blinded status of the neurologic examiners and the fact that toxicology screens were used in addition to histories to determine cocaine use. However, this study also was conducted in an inner city hospital serving primarily low socioeconomic status (SES) women and information on confounding polydrug use by mothers was considered either somewhat unreliable or was unavailable to the researchers.

Alternately, Hadeed, and Siegel (1989), when studying neonates of 56 mothers who used cocaine prenatally, found no differences in the frequency of maternal preeclampsia or caesarian section (C/S) rate, teratogenicity, narcotic withdrawal symptoms, or illnesses compared to a no illicit drug control group. Alternately, weight, length and head circumference growth curves of infants born to cocaine-using mothers shifted below the 25th percentile, although this finding was not thought to be clinically significant. In addition, cocaine use did seem to precipitate more spontaneous abortions, abruptio placentae, and meconium stained amniotic fluid. Advantages of this study included the use of a cocaine only group and blinded evaluations. In addition, maternal factors were controlled for differences in age, parity, socioeconomic status (SES), ethnicity, and smoking, making findings apparently more reliable.

One of the most prolific researchers in this area, Ira Chasnoff, consistently reported a number of negative outcomes for infants exposed to cocaine in utero in his early investigations. In addition to the effects described by both Oro and Dixon (1987) and Ryan et al. (1987), Chasnoff (1989) reported a higher incidence of significant genitourinary tract malformations. In one study of a pool of 70 infants with

cocaine-using mothers, Chasnoff (1989) found two infants with prune belly syndrome, (a congenital nephrotic disorder) one with female pseudohermaphroditism, two with hypospadias and undescended testes, and three with hydroureter/hydronephrosis. Further, two infants in this study suffered perinatal cerebral infarctions that he attributed to maternal cocaine use in the 48 to 72 hours preceding delivery.

In a similar study, Chasnoff, Chisum, and Kaplan (1988) found nine of 50 infants born to prenatal cocaine users had some form of physical anomaly compared to only one of 30 infants born to polydrug noncocaine-using women. These anomalies included two with ileal atresia and seven with malformations of the genitourinary tract. While the researchers attributed these effects to cocaine exposure, all women in the study were known substance users specifically enrolled for treatment possibly confounding outcome. and polydrug use was common.

Researchers who have considered the outcome of cocaine-exposed children in the context of other factors have found more moderate results. For example, Bauchner, Zuckerman, McClain, Frank, Fried, and Kayne (1988) assessed the risk of SID among cocaine-exposed infants and found one of 175 prenatally cocaine-exposed infants died of SID and four of 821

unexposed children died of SID. These results suggested to Bauchner et al. (1988) no increased risk of SID among infants exposed in utero to cocaine. They observed that cocaine-using mothers tended to use other drugs and alcohol, and tended to have low birth weight babies. They further noted that SID usually accounts for one to two deaths in a thousand; in poor black groups, the rate may be as high as five to six per thousand.

MacGregor, Keith, Chasnoff, Rosner, Chisum, Shaw and Minogue (1987) again examined the perinatal outcome data of 70 women receiving care at a large urban drug treatment center. In this study, the use of cocaine during pregnancy was associated with younger gestational age at delivery, increase in preterm labor and delivery, lower birth weight and delivery of smaller for gestational age infants. However, no cocaine related differences were found in the incidence of abruptio placentae and congenital anomalies. Further, no differences were noted on the basis of patterns of substance use. Again, problems in this study included the possible biases of unblinded investigators and confounding of polydrug use.

Schneider and Chasnoff (1992) also investigated the motor development of cocaine/polydrug infants at four months of age. Assessing 50 nonillicit drug exposed infants and 74 cocaine-

exposed infants, Schneider and Chasnoff (1992) found significant differences between groups in muscle tone, primitive reflexes and volitional movement with cocaine-exposed infants performing more poorly. Results demonstrated that motor differences were evident in cocaine-exposed infants at a postnatal period beyond the first month of life. As in other studies from the Chasnoff group, mother/infant involvement in a drug treatment program was known by investigators, and subjects in the cocaine group included polydrug users.

In a two year followup, Chasnoff, Griffith, Freier and Murray (1992) investigated the growth and developmental outcome of cocaine-exposed infants. Comparing a cocaine-exposed group (with marijuana and alcohol exposure), a marijuana/alcohol exposed group, and a nonexposed control group, they found that cocaine-exposed children no longer lagged behind nonexposed children in terms of length and weight although the cocaine group and marijuana/alcohol group both lagged in head growth. No differences in performance on the Bayley Scales of Infant Development (BSID) were noted between the three groups. Again, these children were all known to the researchers through a drug treatment program, and polydrug use was a confound. Further, the study sample had a

high rate of attrition. The conclusion that head growth after birth may be a biological marker for drug exposure may be correct; however, this cannot be attributed solely to cocaine exposure in utero, particularly since the marijuana/alcohol but no cocaine group also lagged in head growth.

In the context of longer term development, Azuma and Chasnoff (1993) subsequently assessed the three year outcome of cocaine-exposed children using cognitive and behavioral measures. They found that children prenatally exposed to cocaine were no different from controls in terms of intelligence measured on the Stanford Binet (SBIT). However, statistical modelling using path analysis suggested that drug exposure, home environment and level of perseverance (attention) had direct effects on cognitive function, while head growth and parent report of behavioral functioning did not have a direct effect on test scores. The authors considered this a "best case" outcome study because all women were involved in a treatment program. However, as in the two year followup of the same population, possible biases and confounds existed particularly with regard to subject attrition.

From the same research team, Griffith, Azuma, and Chasnoff (1994) also evaluated the three-year behavioral and

developmental outcome of children prenatally exposed to maternal substances of abuse. Their subjects included 93 children exposed prenatally to cocaine and other drugs, 24 children exposed to polydrugs without cocaine and 25 children who were nonexposed. Drug exposed children had smaller head circumferences than nonexposed children; the polydrug/noncocaine group performed worse than nonexposed children on tasks of abstraction and visual reasoning; the cocaine/polydrug group performed worse on a task of verbal reasoning; and a marijuana group performed more poorly on a task of abstract/visual reasoning. Caregivers also rated drug exposed children as more aggressive than nonexposed children.

The authors concluded that not all substance exposed children suffer the same poor prognosis, and that generalizations about outcome for drug-exposed children need to be qualified pending more thorough investigations of the roles of maternal and environmental factors such as SES levels. Recognizing that cocaine may not account for all negative findings and that bias on the part of researchers and even parents could convolute findings was an important pivot point, not only for this group of researchers but for other investigators in the field as well.

Studies focusing on the behavioral outcome of cocaine-exposed infants present a range of findings and methodology. In a study of fetal behavioral state as a predictor of neonatal outcome, Hume, O'Donnell, Stanger, Killam, and Gingras (1989) performed fetal assessments which included ultrasonographic examination, videotaping and scoring of a behavioral protocol developed by the authors. Abnormal or delayed state behavior was identified in 13 of 20 fetuses exposed to cocaine. State organization was also suspect or abnormal for 16 of 20 exposed newborns, and the disorganized behavioral states in fetuses successfully predicted abnormal newborn behaviors. The authors concluded that cocaine disrupts (CNS) development. Again, problems in this early study included lack of a control group, small sample size, unblinded examiners, and the use of unnormed scales which, because they were developed by the authors for this study, may have led to biased observations.

Davis, Fennoy, Laraque, Kanem, Brown and Mitchell (1992), who were also interested in behavioral outcome, studied 70 children with cocaine exposure in utero who had been targeted by positive urine screen, maternal report, or by doctor/agency notation. All children in the study had been referred to a large inner city hospital for developmental evaluation. Davis

et al. (1992) found significant neurodevelopmental abnormalities including language delay and a high frequency of autism (11.4%) in the cocaine-exposed group. Since autistic disorders have not been linked to alcohol or opiate exposure alone, Davis et al. (1992) attributed their findings to cocaine use. There are obvious deficiencies in this study including the nonblinded status of clinical evaluators, the skewed sampling of clinically referred children, the polydrug use status of the mothers, and the conclusion that results must be narrowly attributed to cocaine exposure in utero.

In a study of 51 cocaine-exposed infants and 60 nonexposed infants targeted by maternal report or positive infant urine screening, Neuspiel, Hochberg, Greene, and Campbell (1991) found no differences on the Brazelton Neonatal Behavioral Assessment Scale (BNBAS) administered between one and three days of age. A second examination at 11 to 30 days of age showed a significant difference in motor functioning in the cocaine-exposed group. However, this difference disappeared when researchers controlled for confounding variables such as perinatal and social factors. No differences were detected in observed maternal or infant behaviors indicating that prenatal cocaine use had no significant impact on maternal/infant interactions.

In a study with variable outcomes, Eisen, Field, Bandstra, Roberts, Morrow, Larson, and Steele (1991) studied 26 target and 26 control infants for the effects of maternal cocaine use on the Brazelton Neonatal Behavior Assessment Scale (BNBAS). Infants were excluded if their mothers used opiates; and mothers were matched for maternal age, ethnicity, gravida, previous abortions, and hepatitis. Cocaine-using mothers were more likely to be tobacco and marijuana smokers and alcohol drinkers.

Results showed no differences between controls and cocaine-exposed infants in sex distribution, gestational age, chronological age, birth weight, birth length or postnatal complications. However, cocaine-exposed infants had smaller head circumferences and more obstetric complications than the nonexposed infants. In addition, cocaine-exposed infants showed more stress behaviors defined as abnormal reflex behavior and autonomic instability on the Neonatal Stress Scale. However, regression analysis showed obstetric complications and maternal alcohol use were the only significant variables that contributed to the variance on the Neonatal Stress Scale. Finally, the cocaine group demonstrated impaired ability to habituate responses to repeated stimuli; regression analysis showed cocaine exposure

to account for a significant amount of the variance in habituation scores. Maternal polydrug use may confound findings somewhat in this study.

In an attempt to improve upon the methodology in the prenatal cocaine exposure literature, Woods, Eyler, Behnke, and Conlon (1993) longitudinally assessed infant behavior using the BNBAS at birth and again at one month. Mothers enrolled in this study were from a rural, low income population with little or no drug treatment. All examinations were performed blindly. Woods et al. (1993) found cocaine-exposed infants had lower birth weights and shorter gestations than controls, a finding typical of many investigations. However, there were no differences in neonatal performance on the BNBAS at birth or at one month of age. These results indicate that not all cocaine-exposed infants show neurobehavioral deficits in the neonatal period.

Again, studies of infant neurobehavior report varying results. For example, Mayes, Granger, Frank, Schottenefeld, and Bornstein (1993) reported that exposed infants had poorer orientation than nonexposed infants, while Richardson and Day (1991) reported no differences on any Brazelton scale. In general, studies documenting birth outcome using repeated BNBAS assessments report a pattern of developmental recovery

over the first few weeks of life for the cocaine-exposed infant (Black, Schuler, & Nair, 1993; Coles, Platzman, Smith, James, & Felix, 1992).

Summary of Literature Review

A review of the literature concerning cocaine effects on fetal development indicates several serious methodological problems in human clinical studies, including probable underreporting of cocaine use and the increased likelihood that cocaine users also use more alcohol and other drugs. There is also the likelihood of confounding of other maternal risk factors that are more common in cocaine-using groups than nonusers such as sexually transmitted diseases (including HIV); previous spontaneous and elective abortions, and less prenatal care; low birth weight infants; polydrug use; poor health and nutrition; and poverty (Dow-Edwards, 1991). Other methodological problems endemic to the literature include a preponderance of unblinded evaluations. Further, most research has concentrated on urban populations and inappropriate control groups and analyses which frequently ignore important environmental and maternal factors.

In terms of specific animal research findings, cocaine generally has no effect on gestational length in the rat, a

few studies report an increase in stillbirth rate, and cocaine appears to reduce litter size but only at the most toxic doses which may not be relevant to human studies. In animals, odor-associated learning appears to be impaired in some studies. Altered neuronal circuits, including nigrostriatal pathway (fine motor tuning) and mesolimbic dopaminergic system (reinforcement), have been also demonstrated. Head size in animals does not appear to be associated with prenatal cocaine use.

While some reports in the human clinical literature suggest that cocaine use during pregnancy is associated with smaller babies, others do not find statistically significant effects on fetal growth. Evidence of decreased length in human fetal growth has been found, but it is unclear whether these results can be attributed to cocaine or to other factors such as maternal malnutrition and hypoxia. Further, no specific constellation of fetal malformations is found with prenatal cocaine use although case reports of craniofacial defects, missing digits, and genitourinary malformations exist (Dow-Edwards, 1991).

Transient neurological deficits have been noted in neonates exposed to cocaine in utero which have included tremors, rigidity, hyperactivity, abnormal EEG, seizures,

abnormal orientation, sensory and motor functions. Most of these problems appear to resolve by six months of age. Some studies have found exposed infants at risk for SID whereas others have not found a significant association with cocaine. Additionally, neonates exposed in utero to cocaine do not appear to suffer from addiction to cocaine which is unlike infants exposed to opiates in utero.

At the present time, reduced length and head circumference appear to be the most consistent findings reported for neonates exposed prenatally to cocaine, and again, these deficiencies are usually resolved by one year of age. There does not appear to be a clinical syndrome which adequately captures the impact of cocaine exposure in utero on the developing human. Individual variation in outcome appears to be the most consistent finding. The methodological difficulties of working with a drug-using population, exaggerated media portrayals of 'crack babies,' and the need to control for investigator bias in studies have added to the confusion evident in the cocaine literature. Thus, while cocaine exposure in utero may reasonably be expected to have deleterious effects on some children, it is not possible at this time to define a syndrome in any, even globally, meaningful way.

PURPOSE OF RESEARCH

While the particular results of studies vary somewhat, reports consistently portray cocaine as an agent strongly implicated in a host of negative outcomes. Further, crack has been singled out as the most potent form of cocaine both in terms of abuse potential and morbid impact (Kaye, Elkind, Goldberg, & Tytun, 1989). Clearly research on the implications of in utero exposure to cocaine, and especially crack, needs to be ongoing and continually refined from a methodological, medical and psychosocial perspective.

At present, long-term followup on the effects of prenatal exposure to cocaine and cocaine derivatives is extremely limited. Because of the variability in outcome cited in the neonatal literature, it remains unclear what long-term impact in utero cocaine exposure may have on the developing child. In the past, the media have portrayed cocaine-exposed infants and toddlers as behaviorally disordered, impulsive, nonempathetic, and autistic, generally without benefit of sound empirical evidence. These prejudices have frequently been supported by biased investigations making hasty unwarranted projections as to future status while ignoring the

very significant presses of poverty, malnutrition and a caregiving environment compromised by addiction. While the potential toxicity of cocaine exposure should be in no way minimized, it has been the recent onus of researchers in this area to produce methodologically sound and conservatively interpreted accounts of the impact of cocaine on the developing infant and toddler. Only recently has sound research on the infant and toddler been possible as prospectively enrolled cohorts mature to preschool age and older. Thus, there are a number of interesting questions to be investigated. Whether the effects linked to cocaine exposure in utero are stable over time, and how they translate behaviorally and developmentally will require increasing attention as these infants mature.

The present study is intended as an initial exploration of some of these developmental issues within improved methodological design. Addressed here is whether toddlers exposed in utero to crack differ from same aged unexposed peers in their level of behavioral and adaptive development.

MATERIALS AND METHODS

Subjects

Subjects were 30 children exposed to crack in utero and 30 nonexposed control children who were part of a large, ongoing, prospective longitudinal research project conducted at Shands Teaching Hospital through the Department of Pediatrics, Division of Neonatology. Subjects were the children of women who were originally recruited predominantly from public health department (PHD) prenatal clinics in two counties in an understudied rural area of north central Florida. Recruitment began in the Fall of 1991. These women represented a range of low to moderate reproductive risk and all were scheduled to deliver at the referral hospital. There was a wide range of drug use with most smoking crack cocaine and few having access to drug treatment.

Criteria for inclusion in the original study were: 1) women over 18 years of age to reduce the confounding influence of perinatal risk known to be associated with pregnancy in the young teenager and to eliminate problems with obtaining informed consent from minors, 2) women with no major illnesses

diagnosed prior to pregnancy that are known to affect pregnancy or developmental outcome or maternal interaction or caregiving, such as diabetes, chronic hypertension, immune complex disease, seizure disorders, mental illness or retardation, etc., 3) women with no history of illegal drug use other than marijuana and cocaine, 4) English speaking, and 5) women who did not use any of the following drugs without a prescription or chronically with prescription: amphetamines, benzodiazepines, barbiturates, opiates, methadone, and methaqualone.

Target subjects were selected during a screening interview from those who admitted any prenatal use of cocaine or had a full toxicology screen positive for metabolites of cocaine; maternal urine specimens were taken at two unanticipated times, study enrollment and delivery. Any patient who during the screening interview denied the use of cocaine, the illicit substances and drugs listed above, and had a negative cocaine toxicology screen were retained in the subject pool as a potential match for a cocaine-using subject. Matching was done within each county health department to equate level of prenatal risk and included the following subject conditions: 1) maternal race: black vs. nonblack; 2) parity: primiparity vs. multiparity; and 3) socioeconomic

status: level of Hollingshead Index. These are factors which have been shown to mediate caregiving and affect outcome of high risk infants.

All subject mothers were interviewed once or twice prenatally and/or at the time of birth, and their surviving infants were evaluated at each followup time. Detailed drug-use histories and psychosocial interviews were done by helpful, nonjudgmental, experienced interviewers. Calendars were used to help women identify timing of use, and probing for drug use details was done about past but not present use in an effort to be less threatening. Infants were assessed one to three times in their first week of life and six more times over three years. Three followup assessments were made in the homes and three in the clinics. All infant assessments were performed by trained, reliable examiners blinded to drug exposure history. Subjects in the present study were seen at three years of age plus or minus eight weeks, and measures included parent report instruments and behavioral observation.

Several variables were chosen for use as covariates during statistical analysis in order to strengthen results including maternal alcohol use, maternal depression, child gender, and home environment. Covariates were chosen a'priori based on literature that indicated such variables correlate

significantly with infant/toddler development. Placement in foster care was chosen post hoc to be included as a covariate in the analysis due to the difference in frequency between the two groups and due to the potential impact of foster placement on child outcome at three years of age. Foster care was defined as a child being placed in a home away from, or with a relative other than, their biological mother. Thus, five variables (alcohol use, maternal depression, child gender, home environment, and foster placement) were included as covariates in the initial analyses between groups.

In order to further strengthen the analyses, subjects were excluded from the study based on several birth characteristics which could significantly skew results. These included any child born with a birth weight below 2,500 grams and/or a congenital malformation. Children exposed to cocaine in any form other than crack were also excluded from the study. It was decided a'priori to exclude children from the study who suffered any accident or illness (such as sickle cell anemia) that might seriously affect their performance on developmental measures independent of crack exposure in utero.

Altogether, 90 children from the longitudinal study were evaluated between July 1, 1995 and January 30, 1996. Subjects were assessed in the order that they came in for their three

year followup as part of the ongoing study. Thirteen children (14.4%) were dropped from the study. Of the thirteen excluded children, 9 were low birth weight (69.3%; 5 targets and 4 controls), 3 were exposed to forms of cocaine other than crack (23.1%), and one had sickle cell anemia (7.7%). At the close of enrollment for this study, the matches for 17 (18.9%) of the original 90 had not been tested. Thus, the 17 unmatched subjects had to be dropped from the study.

The remaining 30 pairs of matched children (66.7%) constituted the study sample. Forty of the children (66.7%) were from Alachua County, and 20 children (33.3%) were from neighboring Marion County. Two of the mothers were primiparous (3.3%) and 58 were multiparous (96.7%). Fifty of the mothers were African American (83.3%) and ten were of other ethnic origin (16.7%). Sixteen of the women earned a Hollingshead Index of four (26.7%) while 44 of the women earned a Hollingshead of five (73.3%). The Hollingshead Index is a measure of socioeconomic status based on level of education and employment. Scores range from one to five with scores of four and five representing the lowest levels of employment and education. Thirty of the children (50.0%) were exposed to crack cocaine in utero and 30 were not exposed (50.0%). Tables 1 and 2 outline basic demographic and

covariate characteristics for the sample. For the remainder of this document, 'sample' will refer to the 60 children in this study which was completed in the context of the larger longitudinal study as previously described.

The children in the sample (n = 60) included 34 girls (56.7%) and 26 boys (43.3%). Sixteen children were placed in a home other than that of their biological mother (26.7%). Average birth weight was 3326 grams (SD = 413 grams), and mean age at time of testing was 36.8 months (SD = 1.9 months). The nonexposed group of children was comprised of 18 girls (60.0%) and 12 boys (40.0%). Only two children were in foster care (6.7%). Average birth weight in nonexposed children was 3355 grams (SD = 401.469 grams), and mean age at time of testing was 37.3 months (SD = 1.446 months). The exposed group was comprised of 16 girls (53.3%) and 14 boys (46.7%). Fourteen of the children were in foster placement (46.7%). Average birth weight in exposed children was 3297 grams (SD = 431 grams), and mean age at time of testing was 36 months (SD = 2.3 months).

In the sample, maternal depression scores ranged from one to 43 (M = 19.7, SD = 9.8) with 16 being the clinical cutoff score. Home Environment total scores ranged from 18 to 52 (M = 37.0, SD = 8.4) with a normative sample M = 37.54, SD =

10.41. Alcohol use, calculated as average number of 4-ounce drinks per day over three trimesters, ranged from zero to 3.66 (M = .253, SD = .649). In the nonexposed group, average maternal depression score was 20.9 (SD = 9.5), and average home inventory score was 36.5 (SD = 8.1). Alcohol use in the nonexposed groups averaged .2667 drinks per day (SD = .450). In the exposed group, average maternal depression score was 18.4 (SD = 10.1), and average home inventory score was 37.6 (SD = 8.7). Mean drinks per day in the exposed group was .9333 (SD = .640). For purposes of further analyses, alcohol was coded as a dichotomous variable, either present or absent in the prenatal period.

Parent Report Measures

Vineland Adaptive Behavior Scales

The Vineland (Sparrow, Balla, & Cicchetti, 1984) is a nationally normed measure of adaptive behavior for children birth to adulthood and assesses competency in four skill areas: Socialization, Communication, Motor Skills, and Daily Living. The Survey Form used in this study consists of 297 questions administered to the primary caregiver. Items to be answered on a range from 'yes, usually' to 'don't know' include such examples as "Uses sentences of four or more

words" or "Feeds self with spoon without spilling." Administration time is approximately 15 minutes. Split-half coefficients and test-retest reliabilities for the Adaptive Behavior Composite are .94 and .95 respectively and factors reportedly load in appropriate subdomains of each of the four areas. Scores are percentile ranks, means, and standard deviations.

Connors Parent Rating Scale

The Connors (1990) is a parent rating report of hyperactive and attentional problems in children aged three to 17. It was normed on 383 children and consists of 48 questions which load into six factors including Conduct Problem, Learning Problem, Psychosomatic, Hyperactivity Index, Impulsive-Hyperactive, and Anxiety. Higher scores indicate increased problems in the tested area. Administration time is approximately 15 minutes. Factors loadings of the CPRS-48 range form .41 to .82 and appear stable over time. Scores are percentile ranks, means and standard deviations.

Eyberg Child Behavior Inventory (ECBI)

The ECBI (Eyberg, 1992) is a parent report screening measure for disruptive behaviors in children ages two through

16. It includes an Intensity Scale, which indicates how often the behaviors presently occur, and a Problem Scale, which identifies the specific behaviors that are currently problems for the caregiver. There are a total of 36 items. Clinically, a Problem Scale score of 11 or greater and an Intensity Scale score of 127 or greater are used as cutoffs for disordered conduct. The normative sample was 798 parents of children drawn from six pediatric health care settings sampled so as to approximate the demographic composition of the Southeast. Split-half correlations for both scales were .93. Administration time is approximately 5 minutes.

Behavioral Observation Measure

Dyadic Parent-Child Interaction Coding System-II (DPICS-II)

The DPICS-II (Eyberg, Bessmer, Newcomb, Edwards, & Robinson, 1994) is a direct, objective observation measure to discriminate normal from conduct-disordered child/parent interactions. The system provides a measure of both child and parent behaviors and was originally normed on 20 families referred for treatment of a conduct-problem child and 22 families without such a conduct-problem child. Problem behaviors include disobedience, aggression, destructiveness, or hyperactivity. Reliability for DPICS-II by behavior ranged

from 38% to 99% (Bessmer, 1993). The DPICS-II includes three situations that may be coded. For this study, we selected five minutes of child directed play between caregiver and child (CDI) and five minutes of parent-directed play (PDI).

Administration and scoring criteria for the standardized protocol were not altered. The DPICS-II code categories selected for observation were child behaviors that others have suggested might differentiate between cocaine-exposed children and nonexposed children. Exposed children may demonstrate conduct disordered behaviors. Alternately, the exposed child may be withdrawn in interactive situations. To capture a potential range of child behaviors, both positive and negative, included here were: 1) yell and whine, 2) laugh, 3) destructive, 4) physical negative, and 5) physical positive. These variables were measured by frequency over two, five minute periods. Compliance data were drawn from several variables as follows: 1) compliance or 2) noncompliance to a 3) direct or 4) indirect command, or 5) no opportunity for compliance. Total frequency of commands were calculated for each child. The five compliance variables were also combined to derive a percentage representing the rate of compliance, noncompliance, and no opportunity for compliance for each child. These behaviors are defined in detail in the DPICS-II

manual (Eyberg et al., 1994). Toys used in the play situation were standard and included: 1) large primary-color blocks, 2) a farm, and 3) and a gender-neutral stuffed animal.

Procedures

Parents and children were seen during their scheduled visits as part of the ongoing, longitudinal project. Informed consent was obtained from parents at the intake of the original project approximately three years previously. Maternal demographic and perinatal medical information was obtained from interviews conducted prenatally and/or at the time of birth. Parent report measures for the present study were incorporated into the existing project interview scheduled as part of a home visit when the children were three years old. The play observation for this study was scheduled separately from the parent interview as part of the three-year clinic visit. The observation period was situated in the test period before procedures considered aversive (e.g., physical examination) and after generally nonaversive testing (e.g., Bayley II). Administration of materials was standard for each caregiver/child dyad.

Observation periods were videotaped in a room at either the Public Health Department or delivery hospital. The video

camera was concealed behind a three sided screen to limit distractions and to maximize play opportunity. The three toys were placed in the center of the floor before each video session began. Verbal instructions to the parent for the free play or child-directed play, and for the parent-directed portion of taping were standardized and followed the format provided with the DPICS-II manual.

Tapes were scored by two advanced graduate students trained to reliability on pilot tapes using the DPICS-II (Eyberg et al., 1994) scoring criterion. Examiners were blinded to cocaine status to reduce possible bias.

ANALYSES

Descriptive Analyses

Means and standard deviations were calculated for the total sample for dependent variables including: 1) the Connors' (Connors, 1990) subscales Conduct Problem, Learning Problem, Psychosomatic, Impulsive-Hyperactive, Anxiety, and Hyperactivity Index, 2) ECBI (Eyberg & Colvin, 1994) Problem and Intensity scales, 3) the Vineland (Sparrow et al., 1984) subscales Socialization, Communication, Daily Living, and Motor Skills, and 4) DPICS-II (Eyberg et al., 1994) variables. For the DPICS-II, ten behaviors were chosen for basic frequency observation. For purposes of higher level analyses, four summary variables were derived from DPICS-II compliance data. Normality assumptions for dependent variables were tested by graphing and computing skewness scores. Covariates were included in the initial analyses between groups only for derived summary scores.

Hypothesis 1

To test whether the performance of the entire sample is depressed compared to age-based norms, scores on well normed measures were compared to age-based norms using Welch's V for

unequal n and Studentized Maximum Modulus (SMM) tables for familywise error rates to control for multiple comparisons at the .05 significance level. Dependent variables were grouped conceptually for comparison to norms as follows: 1) the six subscales of the Connors (Connors, 1990) including Conduct Problem, Learning Problem, Psychosomatic, Impulsive-Hyperactive, Anxiety, and Hyperactivity Index, 2) the ECBI (Eyberg & Colvin, 1994) Problem and Intensity scales, and 3) the four subscales of the Vineland (Sparrow et al, 1984) including Socialization, Communication, Daily Living, and Motor Skills.

The ten DPICS-II basic observation frequency variables were broken into two groups for analysis. The first group included compliance information including frequency of direct and indirect commands, compliance, noncompliance, and no opportunity for compliance. The second group consisted of child behaviors including frequency of laugh, yell-whine, physical positive, physical negative, and destructive. Scores were compared to normative data using Welch's V for unequal n and Studentized Maximum Modulus (SMM) tables for familywise error rates. Comparisons to normative groups were not performed for DPICS-II derived summary scores as norms are not available.

Hypothesis 2

It was hypothesized that the performance of the cocaine-exposed group would be impaired compared to the nonexposed group in terms of behavior as measured by parent report on the six subscales of the Connors (Connors, 1990). After graphing to inspect relationships between scales, MANCOVA with Hotelling's T2 was used to analyze between group differences.

Hypothesis 3

It was hypothesized that the performance of the cocaine-exposed group would be impaired compared to the nonexposed group in terms of behavior as measured by parent report on the two subscales of the ECBI (Eyberg & Colvin, 1994). After graphing to inspect relationships between scales, MANCOVA with Hotellings T2 was used to analyze between group differences.

Hypothesis 4

It was hypothesized that the performance of the cocaine-exposed group would be depressed compared to the nonexposed groups in terms of adaptive behaviors as measured by the four subscales of the Vineland (Sparrow et al., 1984) by parent report. After graphing to inspect relationships between

scales, MANCOVA with Hotellings T2 was used to analyze between group differences.

Hypothesis 5

It was hypothesized that the performance of the cocaine-exposed group would be depressed compared to the nonexposed groups in terms of observed disordered behaviors as measured on the DPICS-II (Eyberg et al., 1994). Because data for individual behaviors are observed at very low frequencies, the basic ten observed behaviors were compared for between group differences using t-tests. The four derived summary scores including Total Commands, Percent Compliance, Percent Noncompliance and Percent No Opportunity for Compliance, were treated like parent report variables. After graphing to inspect relationships between scales, MANCOVA with Hotellings T2 was used to analyze between group differences.

RESULTS

Descriptive Analysis

First, means and standard deviations were calculated for the total sample for parent report dependent variables including: 1) the Vineland (Sparrow et al., 1984) subscales Communication, Daily Living, Motor Skills, and Socialization, 2) the Connors' (Connors, 1990) subscales Conduct Problem, Learning Problem, Psychosomatic, Impulsive-Hyperactive, Anxiety, and Hyperactivity Index, and 3) the ECBI (Eyberg & Colvin, 1994) Intensity and Problem scales.

Parent Report Measures

Normality assumptions for parent report dependent variables were then tested by graphing and computing skewness scores. One subscale of the Connors' scale (Psychosomatic) and one subscale of the Vineland (Daily Living) were found to be skewed. These were corrected for further analyses using log transformations. All other dependent variables on standardized parent report measures were found to approximate normality. Data were missing for two children on all Connors subscales, and for one child on all Vineland subscales. Data were missing for four children on the ECBI subscales. Missing

data were substituted with group means to allow analysis of these variables to be performed with equal sample size.

Observational Measures

Second, means and standard deviations were calculated for the total sample for the ten basic frequency observational variables including: 1) DPICS-II (Eyberg et al., 1994) five compliance scores including direct and indirect commands, compliance, noncompliance and no opportunity to comply, and child behaviors including yell and whine, laugh, destructive, physical negative, physical positive, and 2) DPICS-II derived variables as described previously including commands, compliance, noncompliance, and no opportunity to comply.

It was determined a'priori' that the ten DPICS-II observational variables would be consolidated to derive various scores because the frequencies of target behaviors tended to be low. Thus, for the present analysis we were not concerned with testing normality assumptions for the ten individual observational scales. However, normality assumptions for consolidated observational dependent variables including Total Commands, Percent Compliance, Percent Noncompliance, and Percent No Opportunity to comply were tested by graphing and computing skewness scores.

The Total Commands score was derived by adding together total direct command comply, total direct command noncomply, total direct command no opportunity to comply, total indirect command comply, total indirect command noncomply, and total indirect command no opportunity to comply. Percent Compliance was the sum of total direct command comply and total indirect command comply divided by the sum of total direct command comply, total indirect command comply, total direct command noncomply, total indirect command noncomply, total direct no opportunity to comply, and total indirect no opportunity to comply. Percent Noncompliance was the sum of total direct command noncomply and total indirect command noncomply divided by the sum of total direct command noncomply, total indirect command noncomply, total direct command comply, total indirect command comply, total direct command no opportunity to comply, and total indirect command no opportunity to comply. Finally, Percent No Opportunity to Comply was the sum of total direct command no opportunity and total indirect command no opportunity divided by total direct command no opportunity, total indirect command no opportunity, total direct command comply, total indirect command comply, total direct command noncomply, and total indirect command noncomply.

Of the four derived DPICS-II observational scales, only no opportunity to comply was found to be moderately skewed. This scale was corrected for subsequent analyses using a log transformation. The remaining three scales, command, comply, and noncomply, were found to approximate normality. Data were missing for six of the children from the nonexposed group. Because data frequency was low on observational scales, it was considered inappropriate to substitute missing data with group means, and analysis of these variables was performed with unequal sample size.

Reliability of Observational Measures

Interrater reliability calculations were performed for two raters on DPICS-II behavioral variables for both child directed interactions and parent directed interactions (Tables 3 and 4). In general, interrater reliability was very strong using Pearson's Product Moment values ranged from r = .84 to 1.00 across the ten basic frequency observation variables in two situations (parent and child directed play interactions). Pearson's correlations can be inflated or deflated based on the frequency of occurrence. Thus, it was decided to determine interrater reliabilities using agreement of occurrence, agreement of nonoccurrence, and finally the mean

of agree occur and agree nonoccur for low frequency data measured in discrete time intervals (Page & Iwata, 1986).

Percent agreement for occurrence was based on summing the agreement of occurrence across subjects and dividing by the agreement of occurrence plus disagreements across subjects. Percent agreement for nonoccurrence was based on summing the agreement of nonoccurrence divided by the agreement of nonoccurrence plus disagreements across subjects. In the child directed interactions, agreement of a given behavior ranged from 89.10% to 100.00%. Similarly, agreement of occurrence of a given behavior in the parent directed interaction ranged from 85.74% to 100.00%. In summary, interrater reliabilities were strong across all behaviors.

Initial Between-Groups Analyses

Demographic Between Groups Differences

Basic demographic match criteria variables measured on a nominal or ordinal scale were analyzed for significant differences between the exposed and nonexposed groups using Fisher's Chi-Square with the Yates Correction for small sample sizes. Demographic variables included parity, race, county, and Hollingshead Index. Due to matching upon entry to the study and limited variability, it is not surprising that no

significant differences were found between groups on these variables. Similarly, no significant differences on interval scale data using t-tests were found on basic child characteristics including birth weight and age at testing (Table 1).

Covariate Between Groups Differences

Covariates measured on a nominal or ordinal scale were also analyzed for significant differences between the exposed and nonexposed groups using Fisher's Chi-Square with the Yates Correction for small sample sizes. Covariates included child gender, foster care, and alcohol use where alcohol use was converted to an ordinal variable to control for outliers. No differences were found between groups in terms of gender. However, children exposed to crack were significantly more likely to be in foster care than children in the nonexposed group with $X^2(1) = 10.31$, $p = .0013$. Similarly, children who were exposed to crack in utero were more likely to be exposed to alcohol than nonexposed children with $X^2(1) = 13.08$, $p = .0003$.

Remaining covariates measured on an interval scale were analyzed for significant differences between exposed and nonexposed groups using t-tests. These covariates included

maternal depression at the three year visit and HOME (Caldwell & Bradley, 1984) inventory total score at the time of the three year visit. No differences were found in terms of maternal depression or HOME inventory total scores at three years of age using exposure status as the independent variable (Table 2).

Group Differences using Covariates as Independent Variables

Notably, significant differences were found on parent report measures when the groups were defined by covariates. For example, groups were defined by maternal depression based on provided clinical cutoffs (Radloff, 1977), the low group with scores of 16 or less (n = 21) and a the high group with scores over 16 (n = 39) representing elevated depression. The elevated maternal depression group demonstrated more conduct problems $t = -2.57$, $p < .013$, learning problems $\underline{t} = -3.16$, $\underline{p} < .003$, hyperactivity $\underline{t} = -2.55$, $\underline{p} < .014$, and increased intensity of problem behaviors $\underline{t} = -2.42$, $\underline{p} < .019$ (Table 5). Similarly, HOME inventory scores were divided based on a provided normative mean of 37 (Caldwell & Bradley, 1984). The first group (low) was comprised of scores of 37 or less (n = 29) and a second group (high) was comprised of scores of greater than 37 (n = 31) representing more enriched

environments. Findings indicated that the group representing children from less enriched environments had more conduct problems $t = 2.57$, $p < .013$, learning problems $t = 2.25$, $p < .028$, worse socialization $t = -2.75$, $p < .008$, and reduced communication skills $t = -2.07$, $p < .043$ compared to children from relatively more enriched environments (Table 6).

When groups were defined by foster care status, children who were with their biological mothers (n = 44) tended to have significantly more conduct problems $t = 2.25$, $p < .028$ than children living away from their biological mothers (n = 16) (Table 7). Further, when groups were defined by child gender, boys (n = 26) were significantly more likely to display learning problems $t = -2.38$, $p < .021$, and have poorer communication skills than girls $t = 2.05$, $p < .045$. Girls (n = 34) were significantly more likely to feel anxious $t = 2.17$, $p < .034$ than boys (Table 8). Interestingly, although alcohol use was significantly different between exposed and nonexposed groups, no significant differences were found on any parent report measure using alcohol as the independent variable (Table 9).

In terms of observational measures and covariates, no between groups differences were found on the four derived DPICS-II scores when groups were defined by either maternal

depression (exposed n = 36, nonexposed n = 18) or HOME inventory (exposed n = 29, nonexposed = 25). Further, no differences were found on derived DPICS-II observational scales when groups were defined by foster care status (exposed n = 15, nonexposed n = 39), gender (exposed n = 24, nonexposed n = 30), or alcohol use (exposed n = 31, nonexposed n = 29) (Table 9). Together, these results suggest that chosen covariates may have complex relationships with outcome on behavioral measures, and that their selection for inclusion as covariates was warranted.

Initial Correlations

Several additional analyses were done to clarify the nature of relationships between covariates and dependent variables, between pairs of covariates, and between pairs of dependent variables. It should be noted that correlations with nominal, ordinal, and interval data were done with Pearson's Product Moment rather than point biserial correlations as the outcome is identical (Weinberg & Goldberg, 1979).

Covariates and Dependent Variables

The relationships between covariates and dependent variables are presented in Table 10. Notably, elevated maternal depression was significantly related to increased conduct disorder r = .3358, p < .01, learning problems r = .3977, p < .01, and hyperactivity r = .3534, p < .01 on the Connors. Maternal depression was also related to the problem scale of the ECBI r = .3387, p < .01, again suggesting that problem behaviors are more strongly associated with higher levels of maternal depression. Similarly, a more enriched home environment as measured by HOME inventory was significantly related to better communication r = .3488, p < .01. Interestingly, no significant relationships were noted between the ten basic and four derived DPICS-II variables and five measured covariates. It should be noted that a more conservative significance level of .01 was chosen in order to partially control spurious relationships that may results from multiple corrrelations.

Covariates

In general, relationships between pairs of covariates were insignificant using a two-tailed analysis. However, caregivers who were raising foster children reported

significantly less depression $r = -.3363$, $p < .01$ than mothers raising their biological children (Table 11).

Dependent Variables

Not surprisingly, when assessing relationships between pairs of dependent variables across the three parent report instruments (Connors, ECBI, and Vineland), behavioral subscales tended to vary together and adaptive functioning subscales tended to vary together. The ECBI problem scale was significantly related to the Connors conduct problem $r = .5569$, $p < .001$, learning problem $r = .5586$, $p < .001$, impulsivity $r = .4915$, $p < .001$, and hyperactivity scales $r = .6089$, $p < .001$. The ECBI Intensity score was also significantly related to these four Connors subscales with increased intensity associated with conduct problems $r = .6635$, $p < .001$, learning problems $r = .5827$, $p < .001$, impulsivity $r = .6014$, $p < .001$, and hyperactivity $r = .6331$, $p < .001$. Interestingly, the Connors subscale learning problem was negatively correlated to socialization $r = -.4672$, $p < .001$ and communication $r = -.3768$, $p < .001$. In other words, higher levels of learning problems were associated with relatively poor socialization and communication. Higher rates of hyperactivity from the Connors were similarly related to

reduced socialization $r = -.3343$, $p < .001$. Neither ECBI score was related to any measured domain of adaptive functioning (Table 12).

Parent Report and Derived Observational Variables

Of particular interest were relationships between parent report dependent measures and derived observational measures. When examining derived DPICS-II scores, results indicate that noncompliance measured objectively was related to caregiver reports of higher learning problems $r = .3578$, $p < .01$, and reduced daily living skills $r = -.4229$, $p < .01$. Similarly, higher levels of caregiver perceived socialization were positively related to compliance $r = .4384$, $p < .01$ (Table 12).

In terms of child behaviors, yell was positively related to conduct problems and psychosomatic behavior with $r = .4186$, $p < .01$ and $r = .4399$, $p < .001$ respectively. Finally, child destructive behavior was significantly associated with conduct problems with $r = .3846$, $p < .01$. It should be noted that a more conservative significance level of .01 was chosen in order to partially control spurious relationships that may result from multiple correlations. Again, preliminary between

group and correlational findings suggest complex relationships between measured scales (Table 12).

Hypothesis 1

It was hypothesized that the performance of both groups would be depressed on all measures compared to age-based norms. Analyses were performed with sample scores and population norms. To test this, Welch's V for unequal sample size was calculated comparing total sample scores on dependent variables to standardized norms. Dependent variables were grouped conceptually a'priori' and Studentized Maximum Modulus (SMM) tables for familywise error rate were used to control for multiple comparisons at the .05 significance level. Tables 13, 14, and 15 summarize these results.

Connors Parent Rating Scale

The first group was comprised of the six subscales of the Connors including: Conduct Problem, Learning Problem, Psychosomatic, Impulsive, Anxiety, and Hyperactivity Indices. Using the SMM familywise rate for six comparisons, Conduct Problem was significantly different from the population norm $v = 5.03$, $p < .01$ where the mean for the sample was higher than the population mean. According to parent report,

learning problems were also more frequent in the sample than the normative group with $\underline{v}$ = 2.98, $\underline{p}$ < .05. Children in the sample tended to be more impulsive than the normative group where $\underline{v}$ = 6.76, $\underline{p}$ < .01. Similarly, parent report indicated increased hyperactivity in the total sample than in the normative population where $\underline{v}$ = 5.30, $\underline{p}$ < .05 (Table 13).

Eyberg Child Behavior Inventory

The second conceptual grouping was comprised of the two ECBI scores including: Problem and Intensity. Using the SMM familywise rate for two comparisons, the total sample was significantly more likely to display a high intensity of problem behaviors than the normative group where $\underline{v}$ = 2.637, $\underline{p}$ < .05. Despite the high intensity of problem behaviors, caregivers did not endorse items indicating that the behavior posed a significant problem in the home (Table 13).

Vineland Adaptive Behavior Scales

The third group was comprised of the four subscales of the Vineland related to adaptive functioning: Socialization, Communication, Daily Living, and Motor Skills. Using the SMM familywise rate for four comparisons, none of the sample

scores on any of these measured domains were significantly different from provided norms (Table 13).

Observational Ratings

The final two conceptual groupings were comprised of basic objective observational data including: 1) direct commands, indirect commands, compliance, noncompliance and no opportunity to comply, and 2) laugh, yell, physical positive, physical negative, and destructive behavior over the total ten minute play period in two situations including both child-directed and parent-directed play. These results are summarized on Tables 14 and 15.

Using the SMM familywise rate for five comparisons, significant differences were noted in sample scores in the child-directed interaction when compared to normative data. Specifically, the caregivers in the present sample tended to have a higher rate of direct commands than either the clinic referred or nonreferred normative group where $\underline{v} = 8.61$, $\underline{p} < .01$ and $\underline{v} = 9.35$, $\underline{p} < .01$ respectively. The rate of indirect commands was similarly elevated in the sample compared to clinic referred and nonreferred normative groups where $\underline{v} = 4.01$, $\underline{p} < .01$ and $\underline{v} = 3.37$, $\underline{p} < .01$ respectively. Not surprisingly given the higher rates of commands, the rate of

compliance was also significantly higher in the sample compared to both the clinic referred and nonreferred reference groups with $\underline{v}$ = 5.47, $\underline{p}$ <.01 and $\underline{v}$ = 6.61, $\underline{p}$ < .01 respectively. Noncompliance was likewise elevated in the sample group compared to referred and nonreferred group with $\underline{v}$ = 3.24, $\underline{p}$ < .01 and $\underline{v}$ = 3.93, $\underline{p}$ < .01 respectively. Finally, no opportunity for compliance occurred at significantly higher rates in the study sample compared to normative groups including clinic referred where $\underline{v}$ = 7.96, $\underline{p}$ < .01 and nonreferred where $\underline{v}$ = 8.12, $\underline{p}$ < .01.

No significant differences between the study sample, and referred and nonreferred normative groups were noted on child behaviors including yell, physical negative or destructive using the SMM familywise rate for three comparisons. It was not possible to test differences in the rate of laugh and physical positive as normative data were not available for these two variables. Results suggest that overall rates of both indirect and direct commands were elevated in the present study sample which in turn results in higher rates of compliance, noncompliance, and no opportunity to comply (Table 14).

Using the SMM familywise rate for five comparisons, significant differences were found between the study sample

and referred and nonreferred normative groups in the parent-directed interactions (Table 15). Specifically, caregivers in the sample group displayed significantly more direct commands than either the referred or nonreferred normative groups with $\underline{v}$ = 4.91, $\underline{p}$ < .01 and $\underline{v}$ = 7.64, $\underline{p}$ < .01 respectively. Interestingly, no differences were noted in the rate of indirect commands in the parent-directed interaction. As in the child-directed interactions, the rate of compliance was significantly higher in the sample group during the parent-directed interactions than in either the referred or nonreferred normative groups with $\underline{v}$ = 6.13, $\underline{p}$ < .01 and $\underline{v}$ = 5.28, $\underline{p}$ < .01 respectively. Similarly, the study sample tended to have a significantly higher rate of no opportunity to comply than either the referred or nonreferred comparative group with $\underline{v}$ = 3.76, $\underline{p}$ < .01 and $\underline{v}$ = 5.55, $\underline{p}$ < .01 respectively.

Alternately, no significant differences were noted in the rate of noncompliance between the study sample and normative groups. It was not possible to test between groups differences for child behaviors for laugh, yell, physical positive, physical negative or destructive due to either the absence of normative data or variance in the normative group (Table 15). Finally, it should be noted that the significance

for certain comparisons may have been diminished by the use of familywise comparisons which tends to reduce power.

Hypothesis 2

It was hypothesized that behavioral difficulties would be more pronounced in the exposed group. Descriptive data for the exposed and nonexposed children are summarized on Table 16. To test this hypothesis, a multivariate analysis of covariance was performed on the six dependent variables that comprise the Connors: Conduct Problem, Learning Problem, Psychosomatic, Impulsive-Hyperactive, Anxiety and Hyperactivity. In the initial analysis, adjustment was made for five covariates including alcohol, maternal depression, foster care, HOME inventory, and child gender. The independent variable was exposure status (exposed to crack versus not exposed). SPSS* (Norusis, 1987) MANCOVA was used for the analyses with the sequential adjustment for nonorthogonality.

With the use of Hotelling's criterion, the dependent variables were significantly related to the combined covariates, with $F(30,232) = 1.70$, $p < .05$. To investigate more specifically the power of the covariates to adjust the dependent variables, multiple regressions were run with

covariates acting as multiple predictors. None of the covariates provided adjustment to the Conduct Problem or Anxiety subscales of the Connors. However, two of the five covariates, child gender and maternal depression, provided significant adjustment to Learning Problems with beta values of .34 $t(53) = 2.75$, $p < .05$ and .41 $t(53) = 3.27$, $p < .05$ respectively. Maternal depression also provided adjustment to Psychosomatic with a beta value of .30 significantly different from zero where $t(53) = 2.13$, $p < .05$. Similarly maternal depression provided significant adjustment to Impulsivity and Hyperactivity with beta values at .36 $t(53) = 2.60$, $p < .05$, and .36 $t(53) = 2.67$, $p < .05$ respectively. For none of the dependent variables did alcohol, foster care, or HOME inventory provide significant adjustment. These covariates were dropped from further analyses.

The effects of exposure status on the dependent variables after adjustment for significant covariates were investigated in univariate and stepdown analysis. Dependent variables were entered in the following order: Conduct Problems, Learning Problems, Psychosomatic, Impulsivity, Anxiety, and Hyperactivity Indices. In the stepdown analysis, each dependent variable was analyzed in turn with higher priority dependent variables treated as covariates and with the highest

priority dependent variables tested in a univariate ANOVA. Conduct Problem was chosen as the highest priority dependent variable since the literature suggests that this may be a marker of prenatal cocaine exposure.

The results of this analysis are shown in Table 17. The Hotelling's criterion for the combination of dependent variables was not significant with $F(6,51) = 1.26$, $p > .05$. Findings indicate that there are no differences between exposed children and nonexposed children on this combination of variables by parent report. Even in a univariate context at the $p < .05$ level, there are no significant differences between exposed and nonexposed children on these variables. Specifically, no significant differences were found between groups for conduct problem $F((1,56) = 1.06$, $p > .05$, learning problem $F(1,55) = 1.22$, $p > .05$, psychosomatic $F(1,54) = .74$, $p > .05$, impulsivity $F(1,53) = .55$, $p > .05$, anxiety $F(1,52) = 3.25$, $p > .05$, or hyperactivity $F(1,51) = .71$, $p > .05$.

Hypothesis 3

As before, it was hypothesized that behavioral difficulties would be more pronounced in the exposed group. Descriptive data for the exposed and nonexposed children are summarized on Table 16. To test this, a multivariate analysis

of covariance was performed on the two dependent variables that comprise the ECBI: Problem and Intensity Scales. In the initial analysis, adjustment was made for five covariates including alcohol, maternal depression, foster care, HOME inventory, and child gender. The independent variable was exposure status (exposed to crack versus not exposed to crack in utero). SPSS^{x} MANCOVA was used for the analyses with the sequential adjustment for nonorthogonality.

With the use of Hotelling's criterion, the dependent variables were not significantly related to the combined covariates with $F(10,102) = .921$, $p > .05$. Thus, all five covariates were dropped from further analyses. The effects of exposure status on the dependent variables without inclusion of covariates were investigated in univariate and stepdown analysis using SPSS^{x} MANOVA. Dependent variables were entered in the following order: Problem Scale and Intensity Scale. In the stepdown analysis, each dependent variable was analyzed in turn with higher priority dependent variables treated as covariates and with the highest priority dependent variables tested in a univariate ANOVA. The Problem Scale was chosen as the highest priority dependent variable as the literature suggests that behavioral problems may result from prenatal cocaine exposure.

The results of this analysis are shown in Table 18. The Hotelling's criterion for the combination of dependent variables was not significant with $F(2,57) = 1.32$, $p > .05$. Findings indicate that there are no differences between exposed and nonexposed children on this combination of variables by parent report. Inspection of univariate and stepdown results at the $p < .05$ level reveal no significant differences between exposed and nonexposed children on these variables. Specifically, groups were not significantly different on either the ECBI problem scale $F(1,58) = 2.63$, $p > .05$, or intensity scale $F(1,57) = .05$, $p > .05$.

Hypothesis 4

It was also hypothesized that adaptive difficulties would be more pronounced in the exposed group. Descriptive data for the exposed and nonexposed children are summarized on Table 16. To test this, a multivariate analysis of covariance was performed on the four dependent variables that comprise the Vineland: Socialization, Communication, Daily Living, and Motor Skills. In the initial analysis, adjustment was made for five covariates including alcohol, maternal depression, foster care, HOME inventory, and child gender. The independent variable was exposure status (exposed to crack

versus not exposed to crack in utero). SPSS^x MANCOVA was used for the initial analyses with the sequential adjustment for nonorthogonality.

With the use of Hotelling's criterion, the dependent variables were not significantly related to the combined covariates, with $F(20,194) = 1.55$, $p > .05$. Thus, all five covariates were dropped from further analyses. The effects of exposure status on the dependent variables without inclusion of covariates were investigated in univariate and stepdown analysis using SPSS^x MANOVA. Dependent variables were entered in the following order: Socialization, Communication, Daily Living, and Motor Skills. In the stepdown analysis, each dependent variable was analyzed in turn with higher priority dependent variables treated as covariates and with the highest priority dependent variables tested in a univariate ANOVA. Socialization was chosen as the highest priority dependent variable as the literature suggests that social relatedness may be disturbed by prenatal cocaine exposure.

The results of this analysis are shown in Table 19. The Hotelling's criterion for the combination of dependent variables was not significant with $F(4,50) = 1.17$, $p > .05$. These findings suggest that there are no differences between exposed and nonexposed children on this combination of

variables by parent report. Inspection of univariate and stepdown results at the $p < .05$ level likewise reveal no significant differences between exposed and nonexposed children on these variables. Specifically, no significant between groups differences were noted for socialization $F(1,58) = .40$, $p > .05$, communication $F(1,57) = .51$, $p > .05$, daily living $F(1,56) = 1.12$, $p > .05$, or motor skills $F(1,55) = 1.67$, $p > .05$.

Hypothesis 5

Finally, it was hypothesized that disordered behaviors by objective observation would be more pronounced in the exposed group. Descriptive data for the exposed and nonexposed children are summarized on Table 16 collapsed across parent- and child-directed interactions. To test this, a multivariate analysis of covariance was performed on the four dependent variables derived from compliance data on the DPICS-II: Total Commands (frequency data), and Percent Comply, Percent Noncomply, and Percent No Opportunity to comply (percentages). The ten basic DPICS-II frequency observation variables were not tested as they were not normally distributed. In the initial analysis, adjustment was made for five covariates including alcohol, maternal depression, foster care, home

inventory, and child gender. The independent variable was exposure status (exposed to crack versus not exposed to crack in utero). SPSS^{x} MANCOVA was used for the initial analyses with the sequential adjustment for nonorthogonality.

With the use of Hotelling's criterion, the dependent variables were not significantly related to the combined covariates, with $F(20,142) = .229$, $p > .05$. Thus, all five covariates were dropped from further analyses. The effects of exposure status on the dependent variables without inclusion of covariates were investigated in univariate and stepdown analysis using SPSS^{x} MANOVA. Dependent variables were entered in the following order: comply, noncomply, no opportunity to comply, and commands. In the stepdown analysis, each dependent variable was analyzed in turn with higher priority dependent variables treated as covariates and with the highest priority dependent variables tested in a univariate ANOVA. Comply was chosen as the highest priority dependent variable as the literature suggests that child compliance may be disturbed by prenatal cocaine exposure.

The results of this analysis are shown in Table 20. The Hotelling's criterion for the combination of dependent variables was not significant with $F(4,42) = .876$, $p > .05$. These findings suggest that there are no differences between

exposed and nonexposed children on this combination of variables by parent report. Inspection of univariate and stepdown results at the $p < .05$ level likewise reveal no significant differences between exposed and nonexposed children on these variables. Specifically, significant differences were not found between groups for commands $F(1,45) = .26$, $p > .05$, comply $F(1,44) = .86$, $p > .05$, noncomply $F(1,43) = .11$, $p > .05$, or no opportunity $F(1,42) = .02$, $p > .05$.

Table 1

Demographic Characteristics of the Total Sample

MATERNAL	Non-Exposed	Exposed	%	df	p-value
County[a]					
Alachua	20	20	66.7		
Marion	10	10	33.3	1	1.0000
Hollingshead[a]					
Four	8	8	26.7		
Five	22	22	73.3	1	1.0000
Race[a]					
Black	25	25	83.3		
Non-Black	5	5	16.7	1	1.0000
Parity[a]					
Prima	1	1	3.3		
Multi	29	29	96.7	1	1.0000

CHILDREN	Non-Exposed	Exposed	df	p-value
Birthweight (gm)[b]	3355	3297	56	.600
Test Age (months)[b]	37.3	36	56	.056

[a] Using Fisher's Chi-Square with the Yates correction for small sample sizes

[b] Using Student's t-test

* = $p < .05$

Table 2

Covariate Characteristics of the Total Sample

NOMINAL/ ORDINAL	Non-Exposed	Exposed	%	df	p-value
Child Gender[a]					
Female	18	16	56.7		
Male	12	14	43.3	1	.7945
Fostercare[a]					
Yes	2	14	26.7		
No	28	16	73.3	1	.0013*
Alcohol[a]					
Yes	8	23	51.7		
No	22	7	48.3	1	.0003*
INTERVAL	Non-Exposed	Exposed	t	p-value	
Maternal Depression[b]	18.4	20.9	.99	.326	
HOME Inventory[b]	37.6	36.5	-.52	.605	

[a] Using Fisher's Chi-Square with the Yates correction for small sample sizes

[b] Using Student's t-test

* = $p < .05$

Table 3

Reliability of Video Coding of Selected DPICS-II Categories in the Child-Directed Interaction

	r	%Agree Occur	%Agree Nonoccur	Disagree	Mean
Direct Command	.99	95.03	96.16	.26	95.59
Indirect Command	.98	90.18	95.03	.29	92.60
Compliance	.97	93.56	97.44	.12	95.50
Noncompliance	.84	94.19	97.00	.09	95.59
No Opportunity for Compliance	.99	89.32	95.14	.29	92.23
Laugh	1.00	100.00	99.68	.02	99.84
Yell	1.00	100.00	100.00	.00	100.00
Physical Positive	.89	89.10	98.90	.04	94.00
Physical Negative	1.00	100.00	100.00	.00	100.00
Destructive	.98	100.00	100.00	.00	100.00

Percent agreement for occurrence is based on summing the agreements across subjects and dividing by the agreements plus disagreements across subjects. Similarly, percent agreement for nonoccurrence is based on summing agreements across subjects and dividing by the agreements plus disagreements across subjects.

Table 4

Reliability of Video Coding of Selected DPICS-II Categories in the Parent-Directed Interaction

	r	%Agree Occur	%Agree Nonoccur	Disagree	Mean
Direct Command	.99	90.63	96.16	.24	93.39
Indirect Command	.95	85.74	96.35	.38	91.04
Compliance	.97	91.88	96.68	.18	94.14
Noncompliance	.98	90.20	98.40	.11	94.34
No Opportunity for Compliance	.98	86.85	93.12	.35	89.98
Laugh	.99	100.00	99.62	.02	99.81
Yell	.98	100.00	100.00	.00	100.00
Physical Positive	.99	96.15	100.00	.00	98.07
Physical Negative	1.00	100.00	100.00	.00	100.00
Destructive	.97	91.66	100.00	.00	95.83

Percent agreement for occurrence is based on summing the agreements across subjects and dividing by the agreements plus disagreements across subjects. Similarly, percent agreement for nonoccurrence is based on summing agreements across subjects and dividing by the agreements plus disagreements across subjects.

Table 5

Between Group Differences Defined by Maternal Depression

MATERNAL DEPRESSION	Low M (n = 21)	High M (n = 39)	p
CONNORS			
Conduct	53.4286	63.2564	.013*
Learning	48.3810	58.9744	.003*
Psychosomatic	49.2381	54.4103	.217
Impulsive	55.9524	58.9487	.193
Anxiety	49.9048	51.5128	.502
Hyperactivity	53.5714	62.0769	.014*
ECBI			
Problem	7.3810	11.5385	.069
Intensity	107.5238	126.9231	.019*
VINELAND			
Socialization	102.6190	96.8462	.108
Communication	102.6190	102.1026	.882
Daily Living	105.4286	104.1026	.775
Motor Skills	97.0952	96.3333	.856

(Continued)

Table 5 - - Continued

MATERNAL DEPRESSION	Low M (n = 18)	High M (n = 36)	p
DPICS-II (Derived Scores)			
Total Commands[a]	46.0256	46.1333	.989
Percent Comply[b]	.3460	.3514	.908
Percent Noncomply[b]	.0996	.0896	.696
Percent No Opportunity[b]	.5544	.5591	.915

* = $p < .05$

[a] frequency data

[b] percentages

Table 6

Between Group Differences Defined by HOME Inventory

HOME INVENTORY	Low M (n = 29)	High M (n = 31)	p
CONNORS			
Conduct	64.6552	55.2903	.013*
Learning	59.1379	51.6452	.028*
Psychosomatic	55.2759	50.0968	.195
Impulsive	58.6552	57.1935	.508
Anxiety	52.6897	49.3226	.138
Hyperactivity	62.0690	56.3226	.085
ECBI			
Problem	11.7586	8.5161	.140
Intensity	127.0000	113.7097	.095
VINELAND			
Socialization	94.2414	103.1935	.008*
Communication	98.8621	105.4839	.043*
Daily Living	104.0000	105.0968	.804
Motor Skills	92.8621	100.0968	.067

(Continued)

Table 6 - - Continued

HOME INVENTORY	Low (n = 25)	High M (n = 29)	Mp
DPICS-II (Derived Scores)			
Total Commands[a]	45.8000	46.2759	.945
Percent Comply[b]	.3316	.3651	.445
Percent Noncomply[b]	.0947	.0914	.892
Percent No Opportunity[b]	.5738	.5435	.458

* = $p < .05$

[a] frequency data

[b] percentages

Table 7

Between Group Differences Defined by Foster Care Status

FOSTER CARE	No M (n = 44)	Yes M (n = 16)	p
CONNORS			
Conduct	62.3182	52.9375	.028*
Learning	55.6818	54.1250	.692
Psychosomatic	54.1364	48.3750	.202
Impulsive	58.3864	56.5625	.464
Anxiety	51.6818	48.9375	.287
Hyperactivity	59.8409	57.0625	.465
ECBI			
Problem	11.1136	7.2500	.119
Intensity	123.3636	111.2500	.180
VINELAND			
Socialization	99.7727	96.3750	.385
Communication	102.8182	100.8125	.593
Daily Living	105.9545	100.7500	.295
Motor Skills	95.6136	99.3125	.413

(Continued)

Table 7 - - Continued

FOSTER CARE	No M (n = 39)	Yes M (n = 29)	p
DPICS-II (Derived Scores)			
Total Commands[a]	46.0256	46.1333	.989
Percent Comply[b]	.3592	.3247	.481
Percent Noncomply[b]	.0836	.1170	.212
Percent No Opportunity[b]	.5572	.5583	.981

* = $p < .05$

[a] frequency data

[b] percentages

Table 8

Between Group Differences Defined by Gender

GENDER	Girls M (n = 34)	Boys M (n = 26)	p
CONNORS			
Conduct	61.0882	58.1538	.451
Learning	51.8235	59.7692	.021*
Psychosomatic	54.0588	50.6923	.406
Impulsive	57.0294	59.0385	.366
Anxiety	53.0294	48.2308	.034*
Hyperactivity	56.7941	62.1154	.114
ECBI			
Problem	10.2059	9.9231	.899
Intensity	121.3824	118.5000	.732
VINELAND			
Socialization	100.3235	96.9615	.335
Communication	105.1471	98.5385	.045*
Daily Living	105.7647	103.0000	.535
Motor Skills	95.4118	98.1538	.496

(Continued)

Table 8 - - Continued

GENDER	Low M (n = 30)	High M (n = 24)	p
DPICS-II (Derived Scores)			
Total Commands[a]	44.1333	48.4583	.532
Percent Comply[b]	.3746	.3183	.198
Percent Noncomply[b]	.0801	.1089	.233
Percent No Opportunity[b]	.5453	.5728	.500

* = $p < .05$

[a] frequency data

[b] percentages

Table 9

Between Group Differences Defined by Alcohol Use

ALCOHOL	No Use M (n = 29)	Use M (n = 31)	p
CONNORS			
Conduct	63.0000	56.8387	.107
Learning	57.1724	53.4839	.287
Psychosomatic	56.5172	48.9355	.056
Impulsive	59.0000	56.8710	.334
Anxiety	50.7931	51.0968	.895
Hyperactivity	61.8966	56.4839	.105
ECBI			
Problem	11.7931	8.4839	.132
Intensity	127.4438	113.2903	.075
VINELAND			
Socialization	99.1724	98.5806	.865
Communication	100.4483	104.0000	.284
Daily Living	102.6897	106.3226	.410
Motor Skills	96.0690	97.0968	.797

(Continued)

Table 9 - - (Continued)

ALCOHOL	Low M (n = 25)	High M (n = 29)	p
DPICS-II (Derived Scores)			
Total Commands[a]	42.1600	49.4138	.291
Percent Comply[b]	.3690	.3329	.410
Percent Noncomply[b]	.0846	.1000	.524
Percent No Opportunity[b]	.5464	.5671	.611

* = $p < .05$

[a] frequency data

[b] percentages

Table 10

Correlations between Covariates and Behavioral and Adaptive Variables

	Exposure Status	Alcohol Exposure	Foster Care	Gender	Maternal Dep	Home Invent
CONNORS						
Conduct	-.0410	-.1558	-.2830	-.0992	.3358*	.2237
Learning	-.0552	-.0567	-.0522	.2985	.3977*	-.1751
Psychosomatic	-.0825	-.2544	-.1669	-.1093	.3139	-.0869
Impulsive	-.0419	-.0449	-.0962	.1188	.3298	.0158
Anxiety	-.2271	.0114	-.1397	-.2738	.1451	-.1449
Hyperactivity	-.1026	-.1075	-.0961	.2062	.3534*	.1181
ECBI						
Problem	-.1729	-.1245	-.2034	-.0167	.3387*	-.0680
Intensity	-.0114	-.2002	-.1755	-.0468	.3109	-.0656
VINELAND						
Social	.0642	.0123	-.1142	-.1266	-.2017	.3209
Commun	.1101	.1655	-.0704	-.2598	-.0851	.3488*
Daily	-.0794	.1615	-.1373	-.0817	-.1414	.0295
Motor	.1776	.0782	.1078	.0895	-.0737	.2688

(Continued)

Table 10 - - Continued

	Exposure Status	Alcohol Exposure	Foster Care	Gender	Maternal Dep	Home Invent
DPICS-II (Derived Scores)						
Total Commands	.0759	.0274	.0160	.0406	.0333	.0198
Percent Comply	-.1351	-.1070	-.1405	-.1981	-.0207	.0467
Percent Noncom	-.0229	-.0033	.1437	.1883	.1261	.0232
Percent No Opp	.1524	.1110	.0489	.0783	-.0615	-.0627
DPICS-II (Basic Observations)						
Direct Com	.0717	.0236	.0118	.0084	-.0796	.1580
Indirect Com	.1154	-.0155	-.0770	-.0289	-.0576	.2318
Comply	.0415	-.0521	-.0575	-.0656	-.0939	.2127
Noncomply	.0528	-.0094	.0367	.1606	.0543	.0424
No Opp	.1384	.0640	.0162	.0015	-.0890	.1632
Laugh	-.1836	-.0433	-.1050	-.1149	-.1760	-.2549
Yell	-.1523	-.1600	-.0555	.1000	.1736	-.1499
Physical Pos	.0000	.1953	-.0178	-.0642	-.0954	-.0193
Physical Neg	.2432	.2174	.0922	.0700	-.1296	-.0243
Destructive	.0669	-.1305	-.1646	.1516	.2883	-.1774

* $p < .01$

** $p < .001$

Table 11

Correlations between Covariates

	Alcohol Exposure	Foster Care	Gender	Maternal Depression	HOME Inventory
Alcohol	1.0000	.3191	-.0316	-.0928	-.0541
Foster		1.0000	.3093	-.3363*	.0656
Gender			1.0000	-.0830	.0248
Depression				1.0000	-.2629
HOME					1.0000

* $p < .01$
** $p < .001$

Table 12

Correlations between Dependent Subscales

CONNORS	Conduct	Learning	Psycho-somatic	Impulsive	Anxiety	Hyperactivity
ECBI						
Problem	.5569**	.5586**	.2387	.4915**	.1621	.6089**
Intensity	.6635**	.5827**	.2427	.6014**	.0808	.6331**
VINELAND						
Socialization	-.0861	-.4672**	-.1739	-.1941	-.0539	-.3343*
Communication	-.0604	-.3768*	-.1786	-.0780	-.1292	.2737
Daily Living	.0059	-.2056	-.1040	-.2864	-.0352	-.2706
Motor Skills	-.0246	-.1588	-.2236	-.0876	-.3104	-.2185
DPCIS-II (Derived Scores)						
Total Commands	.1053	-.0397	-.0328	-.0731	-.0080	-.0074
Percent Comply	-.0022	-.3005	.0751	-.2315	.1761	-.1646
Percent Noncom	-.1059	.3578*	.2806	.2133	.0304	.2336
Percent No Opp	.0476	.0676	-.2406	.0820	-.1757	.0082

(Continued)

Table 12 - - Continued

VINELAND	Communication	Daily Living	Socialization	Motor Skills
ECBI				
Problem	-.2361	-.1958	-.1177	-.1680
Intensity	-.0862	-.0669	-.1817	-.1364
DPICS-II (Derived Scores)				
Total Commands	.0739	.0544	.0652	.0817
Percent Comply	.2592	.2774	.4384*	.0111
Percent Noncomp	-.2685	-.4229*	-.2757	-.1140
Percent No Opp	-.1637	.0432	-.2942	-.0051

ECBI	Problem	Intensity
DPICS-II (Derived Scores)		
Total Commands	-.1174	-.0110
Percent Comply	-.1527	-.0747
Percent Noncomp	.2771	.1489
Percent No Opp	.0287	-.0250

* $p < .01$

** $p < .001$

Table 13

Means and Standard Deviations of tested Sample with Age-Based Norms - Parent Report

	Sample		Norms	
	M	SD	M	SD
CONNORS				
Conduct	59.82**	14.78	50	10
Learning	55.27*	13.30	50	10
Psychosomatic	52.60	15.39	50	10
Impulsive	57.90**	8.45	50	10
Anxiety	50.95	8.76	50	10
Hyperactivity	59.10*	12.89	50	10
ECBI				
Problem	10.08	8.47	7	8
Intensity	120.13*	30.77	97	35
VINELAND				
Socialization	98.87	13.26	100	15
Communication	102.28	12.70	100	15
Daily Living	104.56	16.90	100	15
Motor Skills	96.60	15.31	100	15

* = $p < .05$

** = $p < .01$

Table 14

Means and Standard Devisations of Tested Sample with Normative Sample - DPICS-II Child Directed Interaction

	Sample		Normative Clinic-Referred		Normative Nonreferred	
	M	SD	M	SD	M	SD
Direct Command	14.48*	9.97	1.90	2.75	1.60	1.60
Indirect Command	2.26*	3.32	.35	.59	.60	.99
Compliance	5.61*	5.13	1.21	1.88	.89	.90
Noncompliance	1.43*	2.24	.36	.63	.17	.51
No Opportunity	9.70*	7.35	1.50	1.40	1.33	1.41
Laugh	.11	.32	--	--	--	--
Yell	.04	.19	.15	.67	.20	.89
Physical Positive	.43	1.00	--	--	--	--
Physical Negative	.02	.14	.00	.00	.00	.00
Destructive	.19	.75	.05	.22	.05	.22

* Sample group significantly different from Clinic-Referred and Nonreferred normative group.

Table 15

Means and Standard Deviations of Tested Sample with Normative Sample - DPICS-II Parent Directed Interaction

	Sample		Normative Clinic-Referred		Normative Nonreferred	
	M	SD	M	SD	M	SD
Direct Command	25.24*	15.50	11.50	8.41	6.75	5.62
Indirect Command	4.15	3.79	6.60	4.00	4.75	3.89
Compliance	10.35*	7.30	3.60	2.32	3.90	3.29
Noncompliance	2.50	2.82	6.10	6.18	1.30	2.29
No Opportunity	16.54*	10.07	8.20	7.89	6.35	5.58
Laugh	.31	1.23	--	--	--	--
Yell	.19	.87	.95	3.34	.00	.00
Physical Positive	.48	1.14	--	--	--	--
Physical Negative	.11	.42	.55	2.23	.00	.00
Destructive	.22	.63	.15	.49	.00	.00

* Sample group significantly different from Clinic Referred and Nonreferred normative group.

Table 16

Dependent Variable Means and Standard Deviations for Exposed and Non-Exposed Children for the Total Sample

	Exposed		Non-Exposed	
	M	SD	M	SD
	(n = 30)		(n = 30)	
CONNORS				
Conduct	57.27	13.05	62.37	16.14
Learning	52.63	12.53	57.90	13.73
Psychosomatic	49.57	12.48	55.63	17.53
Impulsive	57.30	8.04	58.50	8.94
Anxiety	48.57	7.25	53.33	9.58
Hyperactivity	56.37	12.47	61.83	12.94
ECBI				
Problem	8.33	7.81	11.83	8.87
Intensity	116.40	30.32	123.87	31.30
VINELAND				
Socialization	100.20	13.77	97.53	12.84
Communication	104.07	13.33	100.50	12.02
Daily Living	103.10	20.00	106.03	13.30
Motor Skills	99.97	16.46	93.23	13.50

(Continued)

Table 16 - - Continued

	Exposed		Non-Exposed	
	M	SD	M	SD
	(n = 30)		(n = 24)	
DPICS-II (Derived Scores)				
Total Commands	48.6333	22.380	42.8333	28.013
Percent Comply	.3307	.132	.3731	.188
Percent Noncomply	.0981	.093	.0864	.081
Percent No Opportunity	.5711	.123	.5405	.175
DPICS-II (Basic Observations)				
Direct Command	41.5000	21.463	37.5000	25.480
Indirect Command	7.1333	5.237	5.3333	6.418
Comply	16.1000	10.056	15.11672	2.383
Noncomply	4.2333	3.945	3.5417	4.681
No Opportunity	28.3000	15.063	23.6250	17.338
Laugh	.2667	.450	.5833	1.792
Yell	.1333	.434	.3750	1.439
Physical Positive	.9333	1.701	.8750	1.513

(Continued)

Table 16 - - Continued

	Exposed		Non-Exposed	
	M	SD	M	SD
	(n = 30)		(n = 24)	
DPICS-II (Basic Observations)				
Physical Negative	.2333	.626	.0000	.000
Destructive	.3667	.928	.4583	1.668

* = $p < .05$

** = $p < .01$

Table 17

MANCOVA with Covariates Child Gender and Maternal Depression and Dependent Variables from the Connors

	Univariate		Stepdown		
	F	df	F	df	p-value
Conduct	1.06	(1,56)	1.06	(1,56)	.308
Learning	2.27	(1,56)	1.22	(1,55)	.273
Psychosomatic	1.53	(1,56)	.74	(1,54)	.393
Impulsivity	.09	(1,56)	.55	(1,53)	.460
Anxiety	3.89	(1,56)	3.25	(1,52)	.077
Hyperactivity	2.39	(1,56)	.71	(1,51)	.405

Significance not attained in either univariate or step-down context.

Table 18

MANOVA with Dependent Variables from the ECBI

	Univariate		Stepdown		
	F	df	F	df	p-value
Problem Scale	2.63	(1,58)	2.63	(1,58)	.110
Intensity Scale	.88	(1,58)	.05	(1,57)	.819

Significance not attained in either univariate or step-down context.

Table 19

MANOVA with Dependent Variables from the Vineland

	Univariate		Stepdown		
	F	df	F	df	p-value
Socialization	.40	(1,58)	.40	(1,58)	.526
Communication	.91	(1,58)	.51	(1,57)	.477
Daily Living	.16	(1,58)	1.12	(1,56)	.293
Motor Skills	2.67	(1,58)	1.67	(1,55)	.201

Significance not attained in either univariate or step-down context.

Table 20

MANOVA with Dependent Variables from the DPICS-II--Derived Variables

	Univariate		Stepdown		
	F	df	F	df	p-value
Commands	.26	(1,45)	.26	(1,45)	.612
Comply	.84	(1,45)	.86	(1,44)	.358
Noncomply	.02	(1,45)	.11	(1,43)	.744
No Opportunity	1.07	(1,45)	.02	(1,42)	.881

Significance not attained in either univariate or step-down context.

DISCUSSION

Background

This study was designed to explore differences in behavioral and adaptive functioning between toddlers who were prenatally exposed to crack cocaine and their matched nonexposed peers. Results showed that children in the total sample tended to display more conduct problems, learning problems, impulsivity, and hyperactivity than normative samples. Higher intensity of problem behaviors was noted in the total sample compared to norms. During the child-directed interaction portion of the DPICS-II, caregivers in the total sample tended to have a higher incidence of direct commands and indirect commands in conjunction with higher incidence of child compliance, noncompliance, and no opportunity to comply than the normative group. Similarly, during the parent-directed interaction portion of the DPICS-II, caregivers tended to have a higher incidence of direct commands in conjunction with higher incidence of child compliance and no opportunity to comply.

Most interesting were negative findings when comparing exposed to nonexposed children. Results indicated no significant differences between the two groups based on drug exposure status on: 1) the Connors subscales including Conduct, Learning, Psychosomatic, Impulsive, Anxiety, and Hyperactivity, 2) the ECBI Problem and Intensity Scales, 3) the Vineland subscales including Socialization, Communication, Daily Living, and Motor Skills, and 4) on the DPICS-II observational measures including derived scales Total Commands, Percent Comply, Percent Noncomply and Percent No Opportunity in addition to Laugh, Yell, Physical Positive, Physical Negative, and Destructive.

Evidence that cocaine exposure may have at least a short term neurological impact has been described in the literature, including smaller head circumferences, jitteriness, poor orienting and habituation, tone abnormalities, increased aggression, language delays, and even autism (Bingol et al., 1987; Chasnoff, 1989; Chasnoff et al., 1987; Davis et al., 1989; Eisen et al., 1991; Griffith et al., 1994; Hume et al., 1989; Oro & Dixon, 1987). Although neurological involvement in this group has been inconsistently and often unreliably documented, the concern that cocaine may affect neurodevelopment and subsequent behavior is certainly

warranted. Although researchers have speculated about the presence of disordered behavior with cocaine exposure, there has been no long-term followup of exposed children which addresses this issue (Davis et al., 1992; Griffith et al, 1994; Hume et al., 1989). Further, methodological problems in the literature have made interpretation of results difficult. Whether disordered behavioral or adaptive outcome can be attributed to cocaine exposure remains an open question (Dow-Edwards, 1991).

Comparison to Norms

As a starting point, the present study was interested in investigating whether clinical norms provided with standardized psychological measures could be appropriately applied to a study sample which, at least in this case, was comprised of primarily poor, undereducated, African Americans. Thus, hypothesis one was concerned with total sample performance compared to norms. Significant differences were noted. For example, the total sample was more likely to display behaviors consistent with conduct problems, learning problems, impulsivity, and hyperactivity than normative samples. In general, these difficulties were worse with increased maternal depression.

Conduct problem on the Connors scale is characterized by items such as 'sassy to grownups,' 'destructive,' and 'bullies others.' The learning problem subscale is comprised by items such as 'difficulty learning,' and 'fails to finish things.' The impulsivity subscale on the Connors was also elevated in the sample and indicates increased incidence of behaviors such as 'excitable, impulsive,' and 'restless in the squirmy sense.' Elevation on the hyperactivity subscale of the Connors in the sample group is consistent with 'restless, always up and on the go,' and 'distractibility or attention span problem.' Again, all but one of these subscales were positively related to maternal depression but were not related to any other covariate.

Similarly, noted differences on the ECBI between the normative group and the total sample on the Intensity scale were represented by high scores on items such as 'acts defiant when told to do something,' and 'has temper tantrums.' Although the sample was not significantly different from the normative group on the Problem scale of the ECBI, higher ratings on this scale were associated with increased maternal depression. The relationship between maternal depression and problem behaviors in children is reflected in the current findings by parent report. Interestingly, inspection of means

reveals that none of the parent behavior rating subscales on either the Connors or the ECBI fall in the clinically impaired range despite some significant statistical differences from normative groups. Thus, differences between the study sample and normative groups may be largely irrelevant in a clinical context.

The first hypothesis also proposed that the sample would be depressed on measures of adaptive functioning compared to normative groups as measured by the Vineland. No significant differences were found between the study sample and normative groups on subscales including Communication, Daily Living, Socialization, and Motor Skills. Notably, Communication, which is characterized by items such as 'uses sentences of four or more words' and 'follows instructions in the if-then format' was positively associated with a more enriched home environment. Again, the impact of home environment on child functioning is well recognized (Azuma & Chasnoff, 1993; Bee, Barnard, Eyres, Gray, Hammond, Spietz, Snyder, & Clark, 1982; Breitmayer & Ramey, 1986).

Comparisons between the study sample and norms were more complex for observational measures. First, differences were broken out between child-directed and parent-directed interactions. Due to the lack of norms, comparisons were not

completed with composite (derived) scores. For the child-directed interactions, the study sample had a significantly higher incidence of direct commands and indirect commands when compared to both referred and nonreferred normative groups. Given the higher incidence of commands, it is not surprising that the incidence of child compliance, noncompliance and no opportunity for compliance was also elevated in the total study sample when compared to both referred and nonreferred normative groups.

For the parent-directed interactions, the study sample had a significantly higher incidence of direct commands, and subsequently, child compliance and no opportunity for compliance when compared to both referred and nonreferred normative groups. No significant differences were noted between the incidence of indirect commands and noncompliance during the parent-directed portion of the DPICS-II. These findings indicate that caregivers in the total sample tended to use more commands (and especially direct commands in the parent-directed context) regardless of the play situation, which in turn seemed to increase the incidence of child behaviors such as compliance.

It is of particular interest that in the parent-directed context, no differences between indirect commands and

noncompliance were noted from normative groups, but that the higher incidence of direct commands occurred together with an increase in child compliance. These results suggest that basic parenting styles may be different when comparing the study group to the normative sample. Observations suggest that the caregivers in the study group may simple talk more than the caregivers included in the normative samples. These findings may reflect cultural or ethnic differences which may play an important role in parenting style and subsequent child behavior independent of drug use or exposure status.

Measures used in this study were chosen for their good standardization properties and ability to distinguish between groups (Connors, 1990; Eyberg, 1992; Eyberg et al., 1994; Sparrow et al., 1984). Thus, significant differences between the total sample and the normative group on these subscales may be interpreted in several ways. First, the total sample regardless of drug exposure status may not conform to normative groups. If this is the case, measures which commonly form the basis for behavioral and adaptive evaluation, such as the Connors or Vineland, may be misleading when used with this sample or other similar samples comprised largely of poor, undereducated, rural, minority caregivers and their children. The danger of misinterpretation of outcome on

parent report measures may be further compounded by the use of an inappropriate control group. For example, there are studies in the cocaine exposure literature that have used no control group or were comprised of mother-child dyads which were unmatched on a number of important variables such as race, parity, SES, etc. (Little et al., 1989; Oro & Dixon, 1987).

Alternately, some systematic variation in the sample group may account for elevations on these scales and significant differences when compared to norms. Our original hypothesis proposed that any elevations in disordered behaviors by parent report or by observation, or reductions in adaptive functioning would be at least partially accounted for by drug exposure status. Thus, the ultimate finding of no differences between exposed and nonexposed groups on all administered measures is especially intriguing. In other words, variability due to drug exposure status does not account for differences between the total sample and norms. The first critical finding of this study, then, is to highlight the possible deviation from standardized normative samples for reasons other than drug exposure status, and second, to emphasize the danger of basing conclusions on test

outcome without using an appropriate (read matched) control group.

Between Groups Comparisons

When accounting for nonsignificant findings between groups, there are several possible explanations. The most parsimonious is that there are in fact no measurable differences in the behavior or adaptive functioning between children exposed to crack prenatally and their nonexposed counterparts at three years of age. Given the level of scientific and popular press focus on the disordered behavior of cocaine-exposed children, support of the null hypothesis in this case is extremely interesting. This finding suggests that when an appropriate control group is used, group differences potentially attributed to cocaine exposure disappear.

A review of the literature indicates that the most reliable findings in the neonatal period is smaller head circumference and reduced length and birthweight (Chiroboga, 1993; Eyler, Behnke, Conlon, Woods, & Frentzen, 1994; Little & Snell, 1991; MacGregor et al., 1987; Oro & Dixon, 1987). Notably, these differences tend to diminish with time until by one year of age, generally no growth differences remain with the possible exception of head circumference (Chiriboga et

al., 1993; Doberczak et al., 1988; Schneider & Chasnoff, 1992).

Similarly, the behavioral literature in the neonatal period has suggested differences, albeit inconsistently, between exposed and nonexposed children. For example, increased risk for motor dysfunction, poor arousal, and cognitive differences have been reported (Bingol et al., 1987; Chasnoff, 1989; Chasnoff, Burns, et al., 1987;Griffith et al., 1994; Oro & Dixon, 1987; Schneider & Chasnoff, 1992; Singer, Yamashita, Hawkins, Cairns, Baley, & Kliegman 1994). One explanation for nonsignificant differences based on drug exposure in this study is that behavioral differences between groups present in the neonatal period, like growth differences, may be compensated by three years of age. This explanation seems unlikely as no initial growth or behavioral differences were noted between exposed and nonexposed children in the larger study (Eyler, Behnke, Conlon, Wobie, & Woods, in preparation).

Alternately, differences in the behavior or adaptive functioning of exposed children at three years of age may exist but be so subtle as to be either unmeasurable by gross parent report or by observed categories of behavior. Along similar lines, the instruments used in this study may not have

sampled behaviors that are indeed different between groups. Addressing the first point, speculating about differences between groups that are too subtle to be measured with current instruments is interesting but scientifically and clinically meaningless. Again, instruments were chosen for the present study based on their good sensitivity to group differences and broad sampling of behaviors. Measures were also theoretically based on existing literature and the presumed disruptive action of cocaine on the developing child.

It appears unlikely that gross differences in behavioral or adaptive functioning were simply missed due to the use of inappropriate measures. As an interesting aside, none of the subscale means on the Connors or Vineland for either the exposed or nonexposed groups actually fall in the clinically impaired range. Thus, even if significant differences between groups existed in the present study, clinical relevance might be debated. The only scale which approaches significance in the clinically impaired range of behavior is the nonexposed group on the ECBI Intensity Scale by parent report.

This finding is mirrored in nonsignificant trends in the data. Inspection of between groups means on behavioral parent report variables indicates that the nonexposed group means were higher on all six Connors subscales including Conduct,

Learning, Psychosomatic, Impulsivity, Anxiety, and Hyperactivity than the exposed groups. Higher scores on these subscales are consistent with increased behavioral problems. Similarly, both the Problem and Intensity scales on the ECBI are relatively elevated in the nonexposed group indicating higher rates and intensity of disordered behavior by parent report. It should be noted that, although not significant, the nonexposed children tended to be slightly older than exposed children which may result in subtle differences in baseline behavior.

When examining outcome on adaptive functioning, the exposed group tended to have higher scores on Vineland subscales of adaptive functioning such as Socialization, Communication, and Motor Skills. The exception is Daily Living Skills where the nonexposed group tended to display more competence. The tendency for nonexposed groups to display generally worse behavior and adaptive functioning is counter intuitive. Although the differences between groups are not significant, it is possible that with larger samples and more statistical power, some significant differences might emerge.

In terms of basic observational compliance data, there was a tendency for caregivers of exposed children to issue

more direct and indirect commands, and for their children to display proportionally higher incidence of compliance, noncompliance, and no opportunity to comply. However, when looking at percentages rather than frequency, exposed children had higher rates of noncompliance and no opportunity to comply, but a lower rate of compliance when compared to nonexposed children. Thus, while exposed children tend to look better by parent report, objective observation suggests that the behavior of exposed children may be worse than nonexposed children. One explanation for this dissociation is that caregivers of exposed children relax their expectations for compliance. Although these are trends only and do not represent significant differences, they suggest parenting styles and rates of compliance between the two groups may be different.

When evaluating remaining child behaviors, such as laugh, yell, physical negative, physical positive or destructive behavior, no obvious pattern emerges. Again, observed trends do not represent significant differences between groups and must be discussed with caution. Alternately, trends are useful when considering direction for future research. It is possible that with larger samples and more statistical power, significant differences might emerge.

Perhaps the most intriguing explanation for the lack of significant findings lies in the progression of neurodevelopment. Briefly, cocaine works on the monamine system in the brain including the neurotransmitter dopamine, serotonin, and norepinephrine. The monamine pathways are involved in early fetal development by innervating forebrain regions. Cocaine may also have effects on brain development that are region specific. For example, subcortical structures including the basal ganglia, nigrostriatal, and mesolimbic brain may be particularly vulnerable. These systems are involved in cognition, arousal, attention, anxiety, and reinforcement in addition to fine motor control. Subcortical connections with the frontal lobes responsible for attention and the modulation of behavior, are vast and reciprocal. Critical here is the maturation of the frontal subcortical connections by myelination, and in particular, the development of the dopaminergic system which can continue into the third decade of life (Yakovlev & Lecours, 1967). Thus, impairments in subcortical to cortical connections and behavioral correlates may not be fully realized until after puberty.

Covariate Findings

To reiterate the major finding, the results of this study showed no significant differences in the behavior or adaptive functioning between children exposed to crack prenatally and nonexposed matched counterparts. If anything, there is a tendency by parent report for nonexposed children to exhibit slightly worse behavior than exposed children. It was presumed at the outset of the study that scores on measures of child behavior and adaptive functioning by parent report and by direct observation would reflect effects of a complex combination of home, caregiver, and child variables in addition to the possible influence of drug exposure. For this reason, multiple covariates were considered in the analysis including prenatal exposure to alcohol, home environment, maternal depression, foster care status, and child gender. Initial exploration of the relationships between covariates and outcome variables confirmed the appropriateness of their inclusion in the study.

First, drug exposure status was positively related to foster care status and alcohol use during pregnancy. In other words, children exposed to crack in utero were more likely to be exposed to alcohol and to be in a foster care placement (defined as someone other than the biological mother) at three

years of age. However, no significant relationships were noted between drug exposure status and any dependent variable. No significant relationships were noted between alcohol exposure and any dependent variable. No significant relationships were noted between fostercare status and any dependent variable.

Remaining covariates were not significantly related to drug exposure status. However, maternal depression was positively related to Conduct, Learning, and Hyperactivity on the Connors and to the Problem scale of the ECBI. In other words, children of depressed caregivers were more likely to display a range of disordered behaviors than children of nondepressed caregivers. Interestingly, maternal depression was negatively associated with fostercare status. Thus, caregivers who were not biological mothers were less likely to be depressed than biological mothers.

How this relates to ultimate performance on measures of behavior, particularly with regard to the tendency for nonexposed children to display more disordered behavior, is unclear. One suggestion might be to study child outcome based on parenting differences between depressed biological mothers and other less depressed caregivers. Finally, HOME inventory was significantly related to the Communication subscale of the

Vineland indicating that children in more enriched homes have better communication skills at three years of age. Child gender was not significantly related to any dependent variable.

Relationships between covariates and dependent variables and the lack of drug exposure findings highlight the importance of considering parenting and environmental variables when studying outcome for cocaine-exposed children. There are actually few studies in the cocaine literature which have evaluated the impact of parenting and rearing environment on child outcome. Eyler et al. (1994) reported that cocaine-using women tended to suffer more depression, poor self-esteem, and feel less in control of their lives than nonusing controls. Cocaine-using women also experienced significantly more stressful life events than nonusers. Although studies have not reported significant differences in the interactions of depressed mothers with their children in infancy (Black et al., 1993; Neuspiel et al., 1994), by the age of three, chronic maternal depression and/or stressful life events may exert a measurable impact on child outcome.

Finally, in an effort to clarify possible relationships between covariates and dependent variables, exploratory between-groups analyses were made using covariates as

independent variables. Findings showed that the group with higher maternal depression demonstrated more conduct problems, learning problems, hyperactivity, and increased intensity of problem behaviors. This finding mirrors these results already discussed. The group with high HOME inventory scores had fewer conduct problems, learning problems, socialization and communication difficulties. Children with their biological mothers tended to have more conduct problems than children living away from their biological mothers. Finally, boys were significantly more likely to display learning problems and have poorer communication skills than girls, and girls were more likely to feel anxious. No differences were noted by groups when defined by alcohol use versus no alcohol use.

These findings are sensible given our understanding of the effects of parenting and environmental variables on child behavior. Given the complexity of possible interactions between these variables and outcome based on drug exposure, their inclusion as covariates in the study appeared appropriate. Although not relevant to the current study, questions about the interactions between covariates, drug exposure and ultimate behavior and adaptive functioning remain. With the continued collection of data, modeling with regression analysis can help to clarify the relationships

between parenting, the environment, and drug exposure status on child outcome.

Strengths and Weaknesses

The study has several important strengths. First, a variety of possible confounding variables were controlled for between groups including alcohol exposure, foster care status, gender, home environment, and maternal depression. Groups were matched on a number of important variables including race, maternal parity, county (which reflected level of prenatal risk), and socioeconomic status in order to control for overall variance in the sample. Children with significant developmental difficulties, exposure to forms of cocaine other than crack, or who were low birthweight (defined as under 2,500 grams) were excluded from the study.

Biological mothers with a significant psychiatric history, illicit drug use (other than marijuana or crack cocaine), or whose primary language was not English were excluded from the study. Biological mothers were over 18 years of age to reduce neonatal risk associated with pregnancy in the young teenager.

Appropriate statistical controls and analyses were used to make interpretation as clear as possible. Welch's V was

used for the sample to norm group comparisons highlighting significant findings that may otherwise have been obscured. The study was based on the literature and what is currently understood about the effects of cocaine on neurodevelopment and behavior. Measures reflected this understanding, and were well normed with good psychometric properties. Examiners were blinded to drug exposure status minimizing bias effects. As much as possible, evaluations were standardized for each child.

There were also several weaknesses to this study. The sample was relatively small limiting the power of comparisons. Comparisons based on population norms were done using familywise error rates. While this contributes to meaningful interpretation, potentially significant findings may have been obscured. The scope of the study was broad and efforts were made to control for large variable to sample ratios by breaking analyses into conceptually related groups. This resulted in seven separate familywise comparisons for the total sample and four separate MANOVAs for between groups comparisons which can inflate Type I error.

Within the MANOVAs, a hierarchical approach was used to control for shared variance among measured variables. Shared variance was assigned to one variable which can result in

spurious significance in the assigned variable and reduce the power of other comparisons. Multiple correlations based on a small sample can also result in inflated significance. A more conservative significance level (.01) was used to offset this.

Use of marijuana and cigarette smoking, which were not controlled in this study, may have affected outcome. Despite extensive interviewing and toxicology screens, it is possible that the control group may have been contaminated by cocaine either by direct maternal use or via secondhand smoke. Further, it was not possible to determine the effect of varying amounts or timing of cocaine exposure on outcome. At three years of age, any behavioral or adaptive impact due to cocaine exposure may be too subtle to capture on the chosen psychological instruments. Alternately, systematic bias may have been present in the responses of biological vs. nonbiological mothers in the study obscuring potentially real differences. Although for this reason it was critical to include an objective measure of behavior, the infrequency of certain behaviors such as 'cry' may have minimized their usefulness as markers of cocaine exposure.

Suggestions for Further Study

As the children in the study sample grow, it will be interesting to note whether current trends in the data become significant. Alternately, it seems unlikely that clinically significant findings would emerge even with an increase in power. Findings strongly suggest that maternal and environmental variables other than prenatal cocaine exposure may be the most significant contributors to behavioral and adaptive outcome at three years old. Modelling the relationships of maternal and environmental variables in addition to exposure status via regression would be interesting as well as studying the possible interactive effects of current covariates and exposure status to outcome. Examining effects of alcohol exposure, fostercare status, etc. just within the cocaine exposure group would also be interesting. Exploring the relationship of multiple foster placements and types of foster placements on child outcome would also be of interest. In addition, the effect of tobacco use on outcome should be included in further study. Finally, examining the possible dissociation between parent report and observed child behavior may prove very interesting as study continues.

Conclusion

The major findings of this study were two fold. First, there were significant differences between the total study cohort and normative groups on which standardized psychological measures are based. Second, at three years of age, no differences were found between a prenatally crack-exposed cohort on measures of behavior and adaptive functioning when compared to nonexposed matched peers regardless of whether evaluation was by parent report or by objective observation.

These findings have implications for the critical evaluation of previous (and future) studies which fail to employ an appropriate control group, and serve as a caution for the common presumption that toddlers prenatally exposed to crack will automatically display disordered behavioral and adaptive functioning. It will be important to continue to follow this population to determine whether prenatal cocaine exposure has any sleeper effects on the behavior or adaptive functioning of children and to clarify the contribution of a variety of factors to child outcome.

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BIOGRAPHICAL SKETCH

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